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Congress Hotel, Chicago, Illinois, June 5 - 8, 1952

VOLUME XXI NUMBER 3

DISEASES

of the

CHEST

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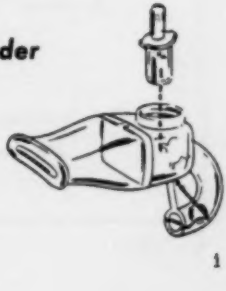

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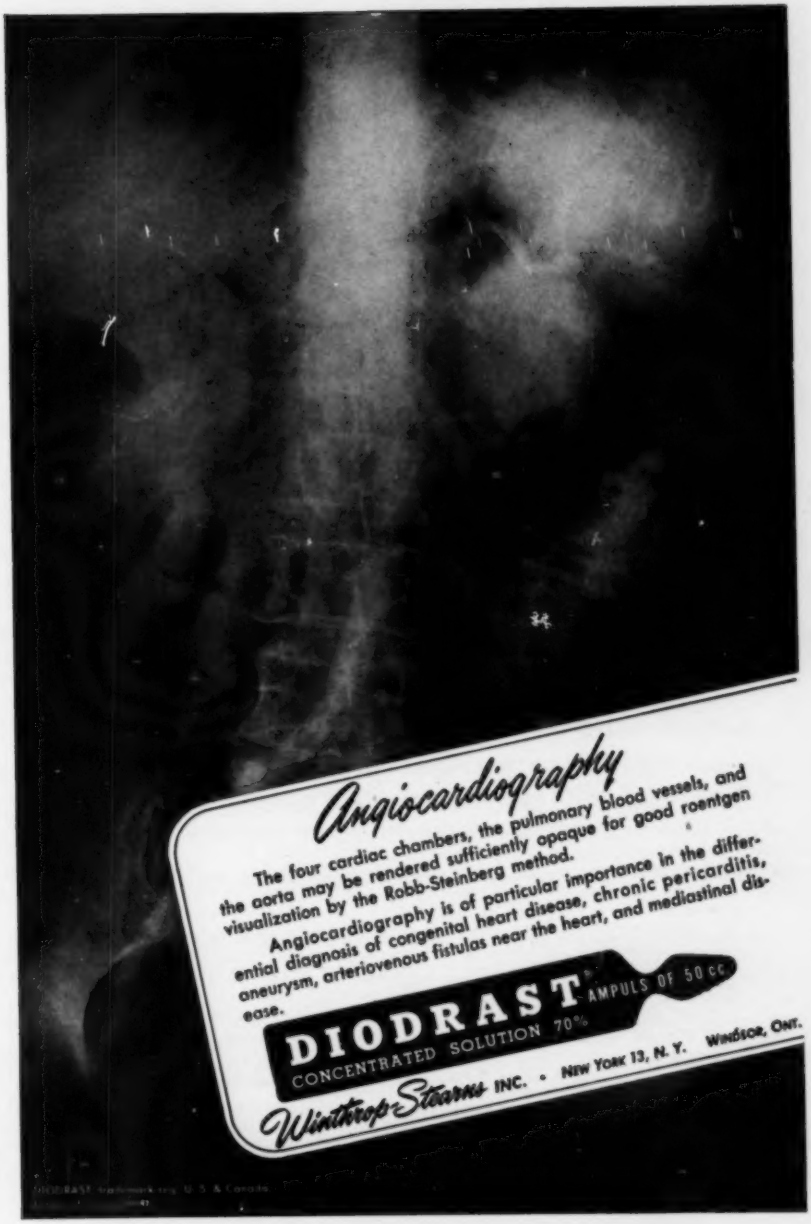
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DISEASES *of the* CHEST

VOLUME XXI MARCH 1952 NUMBER 3

The Use of Trypsin in Chest Disease*

L. C. ROETTIG, M.D., F.C.C.P.,[1] HOWARD G. REISER, M.D.,[2] WILLIAM HABEEB, M.D., F.C.C.P.[3] and LOUIS MARK, M.D., F.C.C.P.[4]
Columbus, Ohio

The almost unprecedented advances in medical and surgical treatment of diseases of the chest which have occurred during the past 25 years have at times led doctors to confusion in treatment and again to neglect of fundamental principles, which have been quite understandable. Nowhere has this been more evident than in the treatment of the various forms of thoracic empyema.

In the 1930's, it was well understood that the treatment of empyema in general involved these fundamental principles: aspiration, adequate drainage at the proper time, and re-expansion of the lung. In advanced, chronic cases where lung re-expansion was impossible empyema space closure was effected by thoracoplasty.

With the development of penicillin and subsequent antibiotics, the new concept of sterilization of the space became possible. This was greatly to be desired, but it frequently led to forgetfulness of the fact that cure of empyema consisted in re-expansion of the lung and return to optimum physiologic activity. As a result

*From the Department of Research Surgery, Ohio State University, College of Medicine; the Department of Pulmonary Diseases, White Cross Hospital, Columbus, Ohio; the Clark County Tuberculosis Hospital, Springfield, Ohio, and the Rocky Glen Sanatorium, McConnelsville, Ohio.

This work was aided by a grant from The Armour Laboratories, Chicago, Illinois.

Presented at the 17th Annual Meeting of the American College of Chest Physicians, Atlantic City, New Jersey, June 7, 1951.

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[2]Resident in Department of Research Surgery, Ohio State University.

[3]Medical Director, Clark County Tuberculosis Hospital.

[4]Chief of Department of Pulmonary Diseases, White Cross Hospital, and Medical Director of Rocky Glen Sanatorium.

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cases frequently were terminated in a state of sterile loculation and fibrothorax, a point of cure far short of optimum.

However, this state of affairs was met by advance in chest surgery. The cases of fibrothorax were submitted to a new and radical decortication, which allowed more or less complete re-expansion and seemed to many an adequate answer.

The surgical advance represented by decortication was then extended to the treatment of tuberculous empyema. Again the results were none too happy. In the enthusiasm to use a new surgical advance, the fact was overlooked that the basic principle which allowed the good results in decortication of non-tuberculous empyema was sterilization of the space. This could not be achieved by streptomycin locally instilled and parenteraly administered. Consequently, decortication was done in a heavily infected field resulting frequently in severe infectious complications postoperatively. The results in terms of curability were little better than the older methods of irrigation and radical thoracoplasty.

It was against this background that the initial investigation of trypsin as an agent for enzymatic debridement was undertaken. It was felt that, if the shaggy pyogenic membrane of the empyema cavity, composed of fibrin and viscid protein debris, could be removed by the proteolytic activity of trypsin, the tubercles and bacteria lodged on the pleural surface might be exposed to treatment with streptomycin. This might enable us to control the infection in the space and make decortication a safe procedure.

In a preliminary report in October 1950,[1] we presented the results in the first six cases of mixed tuberculous empyema. Two of these obtained a complete cure of empyema with the use of trypsin alone. The remaining four showed a decrease in viscosity and clearing of their fluid. Positive fluid turned negative in four cases. Since the preliminary report an additional 10 cases have been treated which are included in this paper.

*The Action of Trypsin**

Pure crystalline trypsin, extracted from the pancreas, is a proteolytic enzyme which does not need enterokinase to activate its proteolytic property as others including Best and Taylor[2] believe.

Tested in vitro, it rapidly dissolves fibrin clot and decreases the viscosity of empyema fluid. As reported by Reiser, Patton and Roettig,[3] it will also digest such other dead tissue as muscle, blood vessels, skin, and fascia. It is important to note that it will only lyse dead tissue. It will not attack a living cell. This is important

*The trypsin used was Tryptar, a pure crystalline trypsin supplied by The Armour Laboratories.

when considering the relative safety in using trypsin as opposed to the proteolytic enzymes of streptococcal origin, against which the body has no anti-enzyme.

When given intrapleurally in normal dogs and rabbits, serosanguinous effusion occurs within four hours. At the same time hemorrhagic pneumonic consolidation occurs subpleurally, limited to a depth of one to two millimeters. Filamentous fibrin adhesions form between the two pleural surfaces. This reaction reaches maximum extent in 24 hours. Complete resolution and absorption of fibrin and pneumonitis then occurs in the next 72 hours. Contrary to the findings of Wells, Morris and Dragstedt,[4] prior administration of benadryl prevents gross evidence of histamin-like reactions.

When administered intrapleurally in fibrino-purulent empyema, trypsin rapidly decreases the viscosity of the fluid (Figure 1). In cases impossible to aspirate, the first post-injection aspiration is accomplished with effortless ease. The fibrin and viscid nucleo-

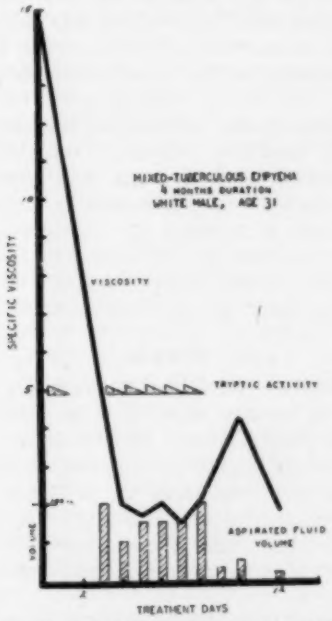

FIGURE 1: Shows the effect of instillation of crystalline trypsin on the viscosity of empyema fluid. (From "Tryptic Debridement of Fibrinopurulent Empyema," Reiser, H. A., Roettig, L. C. and Curtis, A. M., *Surgical Forum*, American College of Surgeons, W. B. Saunders Company, Philadelphia, 1951).

protein of the pyogenic membrane are rapidly digested. The fluid changes from thick pus to a slightly turbid, watery fluid. The turbidity produced by the finely granular digested sediment gradually decreases. After sufficient treatment there results a clear, amber fluid.

The cells of empyema fluid are characteristically fragmented and toxic neutrophils and lymphocytes. After three of four treatments with trypsin these cells disappear and are replaced with normal healthy neutrophils. Between the fourth to seventh day the fluid may become grossly bloody. This occurs as the pyogenic membrane is removed and the new pleural surface exposed. It does not contraindicate continuation of treatment.

Bacteriologic Changes

The changes which occur in the bacteriologic picture of the empyema are of utmost interest. Tubercle bacilli rapidly decrease in number. After the third treatment the smears may be intermittantly negative for several days. The fluid then becomes negative on both smear and culture. This has been true in all but one of the 16 cases on whom treatment has been used. Other bacteria also disappear, so that in mixed cases the entire culture is negative.

Bacteriologic studies thus far indicate that trypsin is not bactericidal. Tubercle bacilli will grow in cultures inoculated with trypsin, as will certain other bacteria. The apparent sterilization of the cavity, therefore, must be accounted for on another basis. The best explanation is probably that trypsin denies to bacteria the culture media needed for growth by digesting the pus and debris of the cavity. It also strengthens the body's humeral defenses by bringing fresh, healthy neutrophils to the surface.

Toxicity

Of equal importance with the bacteriologic changes is the marked decrease in toxicity manifested by all the patients. Daily temperatures in general decrease. Appetite increases, as does general sense of wellbeing. This is best illustrated by Case 6, a semimoribund patient with empyema of 13 years' duration. After trypsin therapy she gained in weight, became afebrile, and was ambulatory for the first time in five years. Decrease in toxicity is of the utmost benefit in preparing these cases for surgery.

Side Effects

Trypsin administered parenterally has a histamine-like reaction. This is manifested by a slight decrease in blood pressure, rise in pulse rate, and elevation of body temperature. The patient may

be protected against this by *prior* administration of an antihistaminic. There has been no evidence of sensitization produced by the drug. In fact, after the third or fourth injection antihistaminics may be discontinued. Transient temperature elevation to 102 degrees F. has been noted in several cases. However, after continued use this reaction disappears. When the drug is re-administered, even after the lapse of a month, no reaction is noted.

Method of Administration

Pure, sterile, crystalline trypsin has been made available in limited quantities for this work. Two hundred and fifty milligrams of trypsin are dissolved in 50 cc. of a sterile solution of Sorensen's Phosphate Buffer. This one-half per cent solution is then administered intra-pleurally.

Prior to administration the patient is prepared with an antihistaminic. This is usually accomplished by giving 20 milligrams of benadryl intravenously 10 minutes before the trypsin, or 50 milligrams of histadyl orally 30 minutes before the trypsin. Following the trypsin 50 milligrams of benadryl or histadyl is given orally every three hours for three doses.

After the patient is prepared, thoracentesis is performed. As much pus as possible is aspirated. The trypsin solution is then injected and the needle withdrawn. The patient is instructed to turn frequently in bed and sit up from time to time.

On subsequent trypsin treatments, aspiration, saline lavage and trypsin instillation is carried out.

Results

The results obtained in 16 cases of empyema have been interesting and most encouraging. Of the entire group four were nontuberculous and 12 were tuberculous or mixed. Of the latter tuberculous group two were negative on smear and culture before treatment began. One re-expanded in 16 days and the other remained completely unchanged.

In our first six cases we had no example of postoperative empyema as a complication of thoracotomy. We could not, therefore, judge the effect of trypsin therapy on the healing of the operative site. We have since had one case of this type, which will be briefly described hereafter. Untoward effects resulting from trypsin therapy in the healing of the chest as a whole were not observed. The empyema was completely cured.

To arrive at a conclusion as to the effectiveness of tryptic debridement, it is first necessary to decide what we wish to achieve. Originally we had hoped to find an agent which would "clean up" the cavity quickly and make the local use of streptomycin effec-

TABLE I: RESULTS IN 17 CASES OF TRYPTIC DEBRIDEMENT FOR EMPYEMA

CASE	Diagnosis	Duration	No. of Trypsin Treatments	Bacteriology	Viscosity	Expansion	Results
1) White Male Age 31	Mixed S. & C. Pos.	4 months	6	Negative 9 days	Decreased 4+	Complete	Cured, 1 year
2) White Female Age 42	Mixed S. & C. Neg.	6 months	10		Decreased 4+	Complete	Cured, 1 year
3) White Female Age 23	Mixed S. & C. Pos.	2 years	3	Negative 3 days	Decreased 4+	One-third complete	Pneumonectomy
4) White Female Age 37	Mixed S. & C. Pos.	13 years	10	Negative 60 days	Decreased 4+	None	Marked reduction in toxicity
5) White Male Age 38	Mixed S. & C. Neg.	4 years	6		Decreased 4+	None	Unchanged
6) White Female Age 24	Mixed S. & C. Pos.	6 years	7	Negative 12 days	Decreased 4+	Slight	Sterile space 1 month later
7) White Male Age 42	Non-Tuberculous Proteus	45 days	5	Negative 4 days	Decreased 4+	Almost complete	Discharged
8) White Male Age 45	Non-Tuberculous B. Coli	6 months (?)	20	Negative after 12 day	Decreased 4+	Almost complete	Moderate residual thickening

TABLE I (Continued)

CASE	Diagnosis	Duration	No. of Trypsin Treatments	Bacteriology	Viscosity	Expansion	Results
9) White Male Age 60	Tuberculous S. & C. Pos.	21 months	9	Negative 4 days	Decreased 4+	Two-thirds complete	Refused further thoracentesis
10) Negro Male Age 32	Tuberculous S. & C. Pos.	3 years +	12	Negative 12 days	Decreased 4+	None	Decortication and cure, 6 months
11) White Female Age 59	Postoperative Empyema Staph. Albus	14 days	6	Negative 5 days	Decreased 2+	Complete	Cured
12) White Female Age 34	Tuberculous S. & C. Pos.	6 months +	6	Negative 6 days	Decreased 4+	Incomplete	Transferred out of Hosp. before finish
13) Negro Female Age 28	Tuberculous S. & C. Pos.	5 months	18	Remains positive	Decreased 2+	Incomplete	Awaiting decortication
14) White Female Age 42	Non-Tuberculous	6 months +	4		Decreased 4+	Incomplete	Decortication
15) White Female Age 32	Tuberculous S. & C. Pos.	2½ years	12	Negative 12 days	Decreased 2+	Pneumo-nectomy	Doing well at 21 days
16) White Male Age 40	Tuberculous S. & C. Pos.	4 years +	12	Negative 9 days	Decreased 4+	Incomplete	Awaiting decortication
17) White Male Age 19	Non-Tuberculous S. & C. Neg.	9 months	1		Decreased	Complete	Cured

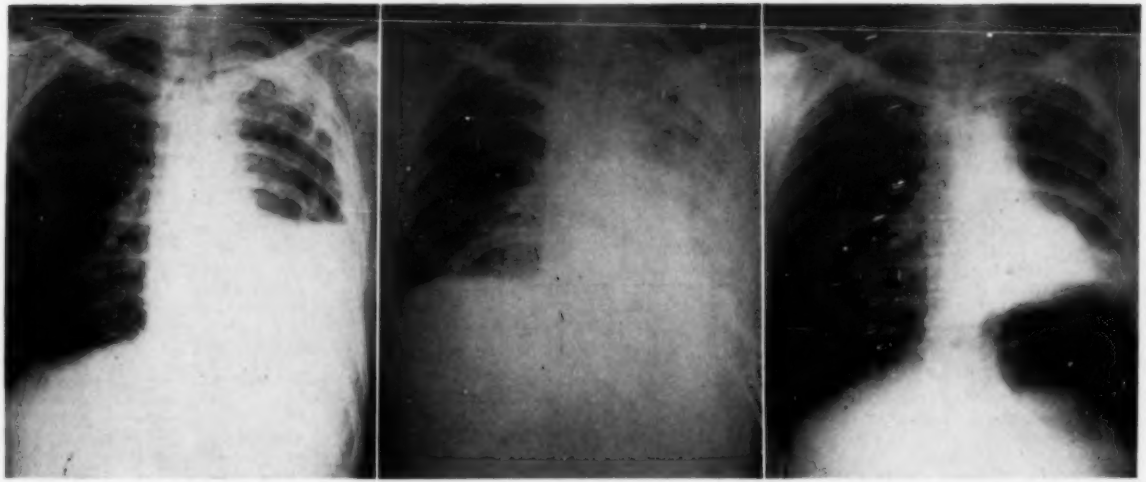

FIGURE 2a FIGURE 2b FIGURE 2c

Figure 2: Roentgenograms of the chest in Case 1, showing complete expansion of the lung and cure of empyema with trypsin alone.

A. Prior to tryptic debridement.

B. During tryptic debridement showing catheter in place.

C. End result. Complete expansion and institution of pneumoperitoneum.

tive. The first two cases in whom it was used, however, showed such startling results that we were for a time led to believe we had found more than we were trying to obtain. The first two cases (Table I) showed complete re-expansion of lungs and healing of empyema on trypsin instillation and aspiration alone. It seemed that trypsin might be a means of debriding, expanding, and sterilizing empyema by itself. Subsequent cases proved this to be only partially true. It is now felt that complete cure with trypsin alone can only be expected if the empyema is of less than six months' duration before excessive scarring occurred.

If, however, we retain our original criteria, namely, a method for quickly debriding and sterilizing the cavity so that decortication or resection can be more safely accomplished, then tryptic debridement has been eminently successful. This success is based on the following points: rapid decrease of viscosity of the empyema fluid, lysis of the pyogenic membrane, and the sterilization of the space.

On the basis of re-expansion of lungs using trypsin alone, six of 17 cases showed a satisfactory result, the longest in duration prior to treatment was six months.

From the standpoint of removal of the pyogenic membrane, we feel that trypsin is definitely effective. We have directly inspected the pleura in five cases. In each case it has been found to be clean and glistening, even when greatly thickened. In one of these cases, which showed complete calcification of the cavity wall, the calcium placques were found at decortication to be loosened from the wall and lying free in the space. In all cases x-ray films showed a decrease in thickness of the space wall.

The viscosity of the empyema fluid was decreased in all 17 cases. This change occurs rapidly and is impressive.

Sterilization of the space was an unexpected development. It was originally planned to follow trypsin treatment with penicillin or streptomycin. Of the 17 cases, 13 had positive smears and cultures at the beginning of treatment. Twelve of these became negative after a period ranging from three to 60 days. The average was about 10 days. One case did not convert and is the only one judged a complete failure.

Five cases were non-tuberculous empyema. Trypsin was most effective in these cases—four re-expanding with trypsin alone, and the fifth, of six months' duration, requiring decortication.

Case Reports

Case 1, R.G.: A 39 year old white male was admitted to Rocky Glen Sanatorium in October 1949, with a diagnosis of moderately advanced pulmonary tuberculosis, bilateral, with left tuberculous empyema. Smears and cultures of the fluid were positive for tubercle bacilli. The empyema

had been present for one month. Three months after admission an intercostal drainage tube was inserted. Daily irrigations with Azochloramide were started. No change was noted. Two weeks later trypsin was instilled into the chest. The following day x-ray film showed the lung completely re-expanded. Five more trypsin treatments were given. At the time of the last treatment the fluid was negative for tubercle bacilli. The tube was withdrawn. One month later pneumoperitoneum was started to control the parenchymal lesion. His sputum became negative and he has now been well for one year (Figure 2).

Case 2, B.J.: A 32 year old Negro male was admitted to the hospital in September 1950, with tuberculous empyema of at least three years' duration. Sputum was negative but empyema fluid was positive for tubercle bacilli. X-ray film showed calcification of the cavity wall (Figure 3). It was almost impossible to aspirate the pus. After one injection of trypsin the cavity was evacuated freely. Twelve irrigations were given and the fluid was negative for tubercle bacilli on the 12th day. Decortication was done the following day. On opening the cavity placques of calcium were found dislodged from the wall, lying free in the space. Postoperatively he made an uneventful recovery, and has been well for six months.

Case 3, B.R.: A 59 year old white woman was admitted to White Cross Hospital in November 1950, for the treatment of esophageal varices. A Phemister type esophago-gastrectomy and splenectomy were performed. An intercostal drain was used and removed in 48 hours. On the 12th postoperative day an elevation in temperature occurred and thoracentesis was performed. The fluid removed was markedly turbid and showed the presence of staphylococcus albus. On the 14th postoperative day the chest was instilled with 200 mg. of trypsin. Four more instillations were

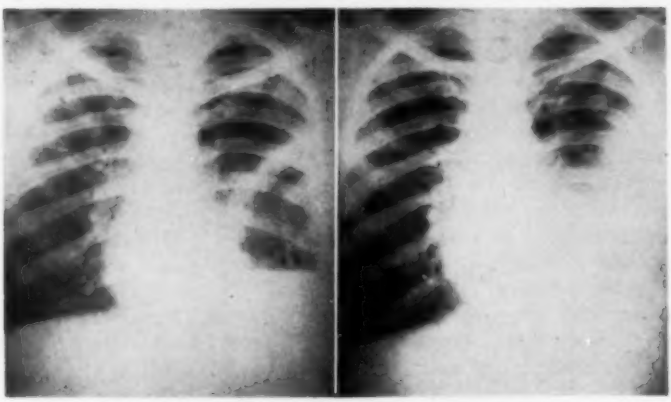

FIGURE 3a FIGURE 3b

Figure 3: Roentgenograms of chest in Case 2, showing the cure of tuberculous empyema following tryptic debridement and decortication.

A. Pre-operative x-ray film showing calcification of cavity wall.

B. Two months following operation. No fluid present. Completely healed.

carried out on alternate days. After the fourth instillation the fluid was found to be sterile. Treatment was then discontinued because the lung was re-expanded. Complete recovery followed. The gastro-esophageal anastomosis was in no way disturbed by the trypsin (Figure 4).

Post-traumatic Fibrothorax

Fibrothorax resulting from clotting of post-traumatic hemothorax should not be allowed to develop but does occasionally occur. It is usually treated satisfactorily by decortication but this entails a major thoracotomy.

In vitro, 350 mgm. of trypsin will completely dissolve a 25 gm. blood clot in 15 minutes. It should, therefore, digest fibrinothorax or clotted chest satisfactorily. Our clinical experience has substantiated this. The following case is illustrative:

Case 18, R.C.: A 51 year old white male was admitted to the hospital in April 1951, with a hemothorax and multiple rib fractures following an automobile accident. He was treated conservatively and discharged on the fifth postoperative day when the fluid seemed to be decreasing. Three weeks later he was re-admitted with "fibrothorax" involving approximately the lower quarter of the left chest. Four instillations of trypsin were carried out. The lung completely re-expanded (Figure 5).

The Use of Aerosol Trypsin

It seemed logical that if trypsin would digest pus it would also lyse the thick respiratory secretions occurring in such conditions as bronchiectasis, tuberculosis, purulent bronchitis, and certain types of asthma.

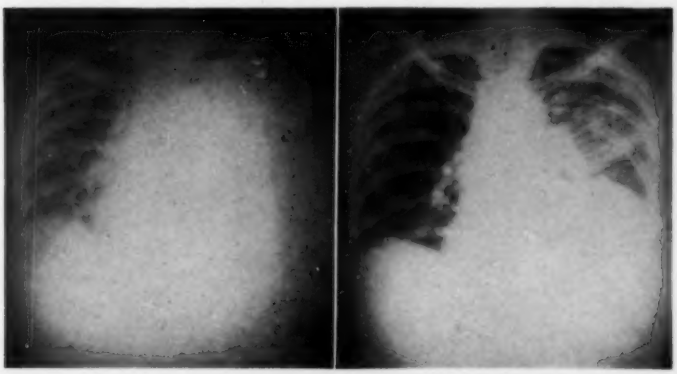

FIGURE 4a FIGURE 4b

Figure 4: Roentgenogram of chest in Case 3. Staphylococcic empyema complicating postoperative recovery from esophago-gastrectomy.

A. X-ray film before tryptic debridement.

B. X-ray film showing complete healing. Diaphragm is elevated by phrenic paralysis performed at time of operation.

Various samples of thick, tenacious sputum were first tested in vitro. Uniformly all were found to be completely digested in 10 to 15 minutes when incubated at 37 degrees C. Microscopic examination showed the strands of mucin to be broken up into small, round globules.

Trypsin was tested for toxicity on a group of 10 rabbits. It was found impossible to kill any of them by insufflating, instilling, or aerosolizing 250 milligrams into the tracheobronchial tree. This was done without any antihistaminic protection. No histamine reaction was encountered.

Aerosol trypsin has thus far been used in 15 persons. A full report on this will be made later. In five treated at one hospital no benefit was obtained. The patients complained of mild dyspnea, low temperature elevation and marked hoarseness. A group of 10 treated at a second hospital, on the other hand, showed a marked decrease in the viscosity of their sputum, followed by an actual decrease in the amount of sputum and an increase in vital capacity. Interestingly enough, it was noted in this group that a marked and significant decrease in the Gaffky count on the sputum occurred.

This second group complained only of mild hoarseness. One of this group, with tuberculous bronchiectasis, has already undergone pneumonectomy. Her bronchial tree was found to be remarkably free from secretions.

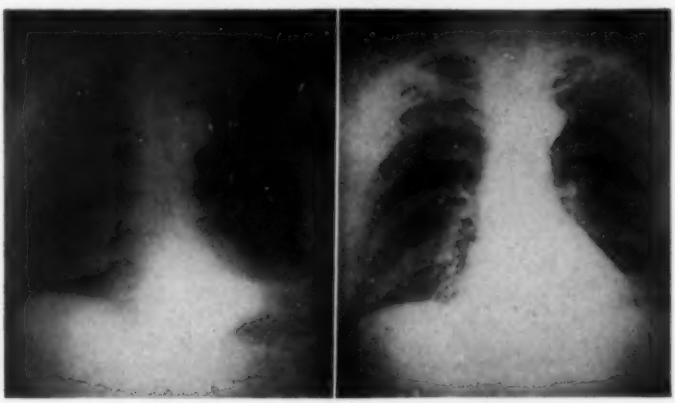

FIGURE 5a FIGURE 5b

Figure 5: Roentgenograms of chest in case of post-traumatic fibrothorax.
A. X-ray film before tryptic debridement.
B. X-ray film after tryptic debridement.

Thus far 100 milligrams of trypsin have been aerosolized once a day in 2 cc. of Sorensen's Phosphate Buffer.

SUMMARY

The use of tryptic debridement in fibrinopurulent empyema is definitely indicated. It quickly removes the pyogenic membrane, decreases the viscosity of the fluid, and in a high percentage of cases sterilizes the space. It thus prepares patients ideally for surgical decortication or resection. In cases of less than six months' duration, tryptic debridement alone may be expected to expand the lung in 65 per cent. It is effective in both tuberculous and non-tuberculous empyema. The incidence of side effects in the nature of histamine-like reaction are few and of minor importance. Complete protection is offered by concomitant anti-histamine therapy. There have been no harmful results, and only one case of 17 is classed as a complete failure. Trypsin can be conveniently packaged, easily handled, and used with a minimum amount of waste.

The use of tryptic debridement in post-traumatic clotted chest will supplant surgical decortication. It can be used in postoperative empyema without fear of damaging the process of tissue repair. Its use in the presence of bronchopleural fistula is not contraindicated.

Results thus far obtained warrant a continued investigation of the use of aerosol trypsin in cases associated with copious, tenacious and purulent sputum.

RESUMEN

El uso de la desbridación tripsínica está definidamente indicado en el empiema fibrinopurulento. Rápidamente quita la membrana piógena, disminuye la viscosidad del líquido, y en un elevado porcentaje de casos, esteriliza el espacio. Así prepara de manera ideal a los enfermos para la decorticación quirúrgica, o para la resección. En casos de menos de seis meses de duración, la desbridación tríptica sola es capaz de lograr la expansión del pulmón en 65 por ciento de ellos. Es efectiva tanto en el empiema no tuberculoso, como en el tuberculoso. La incidencia de efectos colaterales del tipo de las reacciones histamínicas, es baja y de menor importancia. Se obtiene una completa protección contra estos efectos, usando los medicamentos antihistamínicos. No ha habido efectos perjudiciales, y solo un caso entre 17 se ha clasificado como fracaso completo. La tripsina puede ser convenientemente empacada, fácilmente manejada y usada con el mínimo de desperdicio.

El uso de la desbridación tripsínica en el fibrotórax posttraumático substituirá a la decorticación quirúrgica. Puede usarse en

el empiema postoperatorio sin temor de dañar los tejidos en proceso de reparación. Su uso en presencia de fístula-broncopleural no está contraindicado.

Los resultados hasta aquí obtenidos justifican una investigación más adelante sobre el uso de la tripsina en aerosol, en los casos con esputo copioso, tenaz y purulento.

RESUME

L'auteur donne avec précision les indications de l'utilisation de la trypsine dans l'empyème fibrino-purulent. Très rapidement; elle supprime la membrane pyogéne, fluidifie l'épanchement et dans un grand pourcentage des cas, en assure la stérilisation bactériologique. Ainsi les malades se trouvent idéalement préparés pour la décortication chirurgicale de la plèvre.

Dans les cas qui n'ont pas une ancienneté de plus de six mois, l'action de la trypsine à elle seule peut suffire à réaliser l'expansion du poumon dans 65% des cas. Son action est efficace dans les pleurésies purulentes, qu'elles soient tuberculeuses ou non. Des réactions locales à type histaminique sont rares, et de peu d'importance. On peut y pallier totalement en faisant agir parallèlement un traitement anti-histaminique. Il n'y a pas eu de résultats fâcheux, et un seul cas sur 17 peut être considéré comme un échec total. La trypsine est facile à présenter convenablement, très aisément maniable et utilisable sous un petit volume.

L'utilisation de la dissociation par la trypsine des fibrothorax post-traumatiques pourra èviter la décortication chirurgicale de la plèvre. Elle peut être utilisée dans les empyèmes post-opératoires, sans crainte de réveiller les processus infectieux persistent dans le parenchyme. L'existence d'une fistule pleurobronchique ne contre-indique pas son utilisation.

Les résultats obtenus justifient de nouvelles recherches sur l'utilisation de la trypsine en aérosols dans les cas où s'associe une expectoration importante, tenace et purulente.

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COMMENTS

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When the basic experimental work on animals was completed, and a fairly good knowledge as to reaction and toxic effects was established, trypsin was tried on several patients with tuberculous pleural effusions. The first cases treated responded rapidly by clearing of the effusion. The lung expanded rapidly.

The most striking effects were the rapid improvement in the general condition of the patient. Temperatures dropped rapidly, appetite improved, weight increased promptly and there was a general feeling of well being.

Anti-histamines given prior to the administration of trypsin prevented reaction to trypsin.

Some patients developed high fever for a few days. This subsided rapidly and was never a contraindication to continued use of trypsin.

We had hoped that the use of trypsin would be a means of taking care of the non-expandable lungs, especially those who had pneumothorax for a long period of time and developed thick membranes which prevented expansion. The trypsin cleared the debris, thinned the fluid and made it easily removable, but in some cases did not permit full re-expansion of the lung. These had to be handled surgically. The trypsin, however, did prepare the patient for much better surgical results than would have been obtained otherwise.

Because of the fine results obtained in thinning fluids by intrapleural use of trypsin, we decided to try it by nebulization in cases of bronchiectasis and bronchospasms. We found many more toxic reactions. Hoarseness developed plus a feeling of irritation within the bronchial tree, but in some cases bronchospasms were rapidly broken. The mucous which had been tenacious was thinned and easily expectorated, and we felt encouraged by its use. However, before general use by aerosol can be carried out, considerable more work must be done to determine the dosage necessary, the frequency of nebulization, the prevention of toxic reactions and the prevention of the hoarseness which occurred in many patients. Many cases are now being treated by nebulization, and when this work is completed a further report will be given.

Primary Pulmonary Tuberculosis as a Cause of Bronchiectasis in Children*

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A very large percentage of children with the primary complex of tuberculosis are symptomless, and usually these patients show small parenchymal shadows which lead into regional lymph nodes and slowly calcify. However, symptoms may be present, fever being the most common. This is especially true in the cases showing more massive shadows on the roentgen films, the type referred to as epituberculosis. Biggs[1] has recently called attention again to this type of lesion, although in his series only three of 142 patients with primary infection showed massive shadows. In a ward for tuberculous children at the San Francisco Hospital in 1928, about 10 per cent had these shadows, while in 1950 and 1951 the percentage is about 20. There have been on this ward at all times a large number of children of Oriental, Mexican, and Negro parentage, and these groups have been increasing in numbers through the past two decades. They are known to be more highly allergic, as manifested by the size of tuberculin reactions, than children of the white race,[2] which may in part explain the common incidence of massive shadows.

Jones and Cournand[3] in 1933, mentioned enlargement of lymph nodes in primary tuberculosis as being a possible etiological factor in bronchiectasis. Wallgren[4] called attention in 1935 to the frequency of bronchiectasis following primary tuberculosis of the perifocal or epituberculous type, and reported seven such cases within a single year. In 1937 there was reported from our clinic[5] two cases in older children of left lower lobe bronchiectasis with positive sputum following primary tuberculous infection. Brock, Cann, and Dickinson[6] in 1937, suggested that epituberculosis might cause bronchiectasis, and presented a case history. Kent[7] in 1942, demonstrated asymptomatic bronchiectasis in seven out of 10 children who previously had roentgenographic evidence of atelectasis during their primary tuberculosis. About the same time Jones, Rafferty, and Willis,[8] demonstrated a relationship of tuberculosis of the bronchi to atelectasis, and in a follow-up study Jones, Peck,

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and Willis[9] in 1946, showed unequivocal signs of bronchiectasis in 24 such children. This amounted to 70 per cent of 34 who had proved obstructive lesions associated with primary infection. They reported another follow-up of this series in 1950.[10] These authors concluded that pulmonary tuberculosis in children was a common cause of bronchiectasis. Graham and Hutchison[11] in 1947, reported 45 cases of pulmonary collapse during the primary infection in childhood, and in four of these bronchiectasis developed while they were under observation. These authors, as well as Kent,[7] however, believed that collapse does not play an appreciable role in the etiology of infected bronchiectasis. In 1949 Head and Moen[12] discussed complications of calcified hilus lymph nodes, and stated that basically all of the secondary changes are caused by bronchial ulceration, narrowing and occlusion, and that every type of acute and chronic bronchial and pulmonary disease may be simulated by these complications. Recently Rubin and Rubin[13] reported 16 cases of shrunken right middle lobe in adults, presenting strong evidence that in each instance there was a pre-existing tuberculous focus, probably in the regional lymph nodes. In seven of these patients bronchiectasis was demonstrated, and in several other it was suspected.

The following cases are presented as illustrative of the various sites at which atelectasis can contribute to the production of bronchiectasis in children during or after primary infection.

Case 1: R. M., girl, age 3, Mexican. The patient was symptomless. A friend of the family who lived with them when the child was six months old, had later developed open tuberculosis. On survey of the family the child was found to have a positive tuberculin test, and was brought to our clinic. Physical examination was negative except for ringworm of the scalp and a few wheezing sounds over the apices of the lungs. Coccidioidin and histoplasmin skin tests were negative. The sedimentation rate was 21 mm. in one hour (Wintrobe). Roentgenogram showed enlargement of soft tissue density at the right hilus and infiltration into the right apex and first interspace (Figure 1). Laminography showed compression of the right main bronchus from extrinsic pressure of lymph node situated between the trachea, which was pulled over to the right, and the upper margin of the right main bronchus (Figure 2). Gastric lavage was negative on two occasions for tubercle bacilli by smear, culture and guinea-pig inoculation. Nothing was advised except continued observation.

Case 2: W. M., boy, age 6, Negro. At the age of four he entered the hospital for acute illness with fever and cough. Physical examination showed only congenital nystagmus. Roentgenogram showed a massive shadow in the right lobe (Figure 3). Sedimentation rate was 30 mm. (Wintrobe). Tuberculin test was positive. Stomach washings were positive for tubercle bacilli on culture and guinea-pig, and remained positive at intervals of three months for one year. He became rapidly symptomless and did well. When the collapsed lobe partially cleared, three small

cavities were seen (Figure 4). Sedimentation rate was now normal and stomach washings negative, and have remained so to date. Laminagram showed bronchiectasis of the pectoral segment of the upper lobe and a large hilar node pressing on the bronchus of this segment (Figure 5). The patient two years after the initial infection is symptomless except for a marked predisposition to intermittent acute respiratory infections, when rales are usually present throughout the chest.

Case 3: J. H., boy, age 7, white. Since the age of three he had intermittent acute respiratory infections, with temperature of 103 to 104 degrees F. Pneumonia was diagnosed on one occasion, and at the age of four he was under observation at a County Hospital for tuberculosis. About six months ago he began to have three to four day febrile episodes every two or three weeks. The family history revealed that a 12 year old

FIGURE 1

FIGURE 3

Figure 1: Enlargement of soft tissue density at right hilus and infiltration into right apex.—*Figure 3:* Massive shadow in upper right lobe.

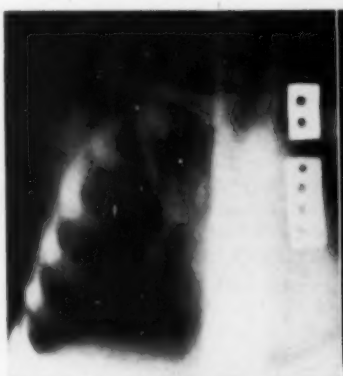

FIGURE 2a

FIGURE 2b

Figure 2: Laminagram showing large lymph nodes at upper right hilus causing collapse and bronchiectasis of upper right lobe (a); with partially calcified node (b).

brother had been diagnosed by roentgenography as having pulmonary tuberculosis. Physical examination revealed some enlarged cervical nodes, and coarse and fine rales over the left base, and left axilla. The spleen was easily felt and reached 8 cm. below the left costal margin. There was slight clubbing of the fingers. The tuberculin test was strongly positive, coccidioidin and histoplasmin tests were negative. The sedimentation rate was 40 mm. (Wintrobe). A liver biopsy showed chronic inflammation. Roentgenographic examination of chest showed heavy shadows in left lung with retraction into the left chest. Bronchograms showed cylindrical bronchiectasis of both branches of the lingula and apical, anterior middle and posterior basal branches of the left lower lobe (Figure 6). Tubercle bacilli were isolated on culture from gastric washings.

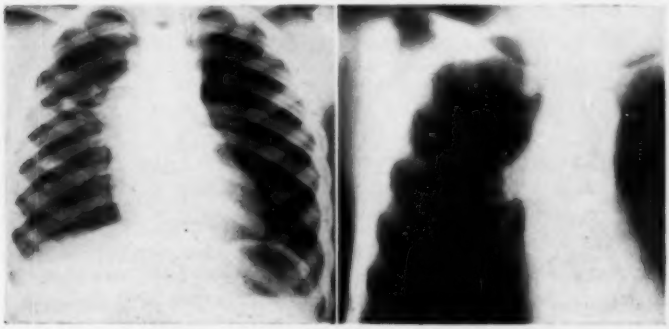

FIGURE 4 FIGURE 5

Figure 4: Two years, 8 months after Figure 3, showing two calcified primary foci, with three small cavities medial to upper focus, and massive hilar nodes.
Figure 5: Laminagram showing bronchiectasis of pectoral segment, with large, partly calcified hilar node pressing on bronchus.

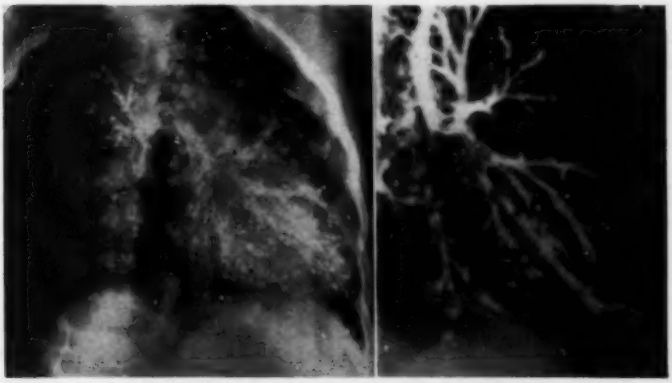

FIGURE 6a FIGURE 6b

Figure 6: (a) Cylindrical bronchiectasis of lingula and left lower lobe.—(b) Spot film of lingula and anterior basal segment of left lower lobe.

Cases 4 and 5: A. F. and E. A. These two girls were first reported in 1937[5] as cases of primary tuberculosis occurring at ages 10 and nine years, followed by bronchiectasis of the left lower lobe in both, and demonstrated by bronchograms at ages of 14 and 13. Both had clinical bronchiectasis with large amounts of sputum and long histories of severe polypoid sinusitis, neither sinusitis responding to surgical treatment. In the sputum of each tubercle bacilli were found constantly until lobectomy was performed, for the first girl in 1938, for the second in 1939. Both had very soon complete and lasting cessation of the symptoms of both bronchiectasis and sinusitis, and tubercle bacilli were never found in sputum or stomach washings following the surgical removal of the affected lobes. The first girl married and had two children, both patients were followed for over five years after lobectomy and were entirely well at the end of this period.

Discussion

In acquired bronchiectasis, the bronchial wall is injured with destruction of the epithelium, loss of cilia and mucous glands, and weakening of both elastic and muscular elements of the bronchus. The contraction of the surrounding connective tissue may contribute to this condition, and dilatation of the bronchi may be caused by peribronchial disease. The resulting stiff tubes are incapable of their normal action.

In bronchiectasis following primary infection, the mucous membrane is conceivably damaged by the infiltration of the elements associated with tuberculin hypersensitivity, which not only swell the interstices of the lung, but also surround the bronchi. The roentgen shadows caused by this process are hardly distinguishable from the true atelectasis caused by extrinsic pressure on a bronchus by peribronchial lymphangitis and lymphadenitis. The latter processes may be expansile or contractile, and may cause ulceration and penetration through the bronchial wall to produce internal occlusion of a bronchus, with subsequent collapse of that portion of a lung. The ultimate result of these different mechanisms, if not corrected, may all be bronchiectasis.

In treatment of this type of bronchiectasis the site of the disease in the lung is of some importance. In general writers on the subject seem to consider the disease in the upper lobes as usually not infectious. Many patients are without symptoms after the tuberculosis has become quiescent, but this is not always true (Case 2). When lesions are in the middle lobe symptoms may be present in childhood, or they may be postponed until adult life, with the possibility that symptoms of bronchiectasis may begin at any time during the life of the individual. In Field's cases[14] of non-tuberculous bronchiectasis in children the lingula was infected in 65.5 per cent, but in not a single case alone. When in the lower lobes from any cause bronchiectasis is seldom silent, and should

be considered the most dangerous to be left untreated. Sinusitis is often present with lower lobe bronchiectasis, and in the tuberculous cases there is a suggestion in some that it may be secondary to the bronchial disease (Cases 4 and 5).

The bronchiectatic lesion itself may be quite removed from the site of the active tuberculous process if the lymph-node causing the bronchial compression is one secondarily infected along the course of the lymphatic drainage, and the collapsed lobe may even be on the opposite side of the chest from the primary focus of infection, and not involve the tuberculous lobe at all.

An attempt should probably be made to expand all collapsed lobes following the initial tuberculous infection, although Field[15] in non-tuberculous cases in children noted no significant difference in the incidence of expansion of the lungs between those treated with bronchoscopy and those treated without it. During the time when the tuberculous process is considered acute, whether bronchiectasis is present or not, the use of streptomycin seems logical, as advocated by Jones and Howard.[16] If bronchiectasis is believed to have already occurred, postural drainage may be of value as supplement to antibiotics in various forms, depending upon the location of the lobe involved.

Surgery is certainly the treatment of choice in any case of chronic symptomatic bronchiectasis in children. The surgeon may be influenced in choosing his time by the acuteness of the tuberculous process, if it be of this type, and by the presence of tubercle bacilli in stomach washings. He need not be influenced greatly by the age of the patient if the latter has passed infancy. The affected lobe is probably a non-functioning one, and as Field states:[17] "The fact that after lobectomy the remaining lung increases its functional capacity in growing children makes it desirable to operate during childhood."

Several authors quoted have noted the common incidence of bronchiectasis following the primary infection of tuberculosis, and Caffey[18] in his textbook emphasizes this fact. Wallgren[4] states that bronchiectases are "commoner than true tertiary pulmonary tuberculosis following primary tuberculosis. The more one is on the lookout for these postepituberculous bronchiectases the more often they will be found." I believe this fact should be re-emphasized often, and that every patient with primary tuberculosis with massive shadows, either of the parenchyma or hilar nodes, should be closely watched throughout his childhood for subsequent bronchiectasis. The use of the term epituberculosis, however, is not adequate in describing the massive shadows which are caused by several different types of lesions not too closely related pathologically.

Since the often benign primary infection may in many children be followed closely by more serious disease, we must not neglect prophylactic measures against tuberculosis in patients, including the separation of open cases of the disease from other children, nor let down in any way in our use of all our safe and proved weapons in combatting this disease.

SUMMARY

1) Bronchiectasis following the primary infection with tuberculosis is a common complication, and should be looked for in the presence of any massive roentgen shadow.

2) Bronchiectasis in the upper lobes is less apt to be symptomatic, but in other parts of the lung demands treatment.

3) Treatment should first be directed toward re-expansion of atelectasis, which predisposes to bronchiectasis.

4) Lobectomy is the treatment of choice when symptoms are present, and should be resorted to in children.

5) The term epituberculous should be dropped as being inadequate to describe shadows that have varied pathological and mechanical implications.

6) The serious character of bronchiectasis as a complication of the primary infection gives added weight to the importance of prophylaxis against tuberculosis, especially in children.

RESUMEN

1) La bronquiectasia después de la primo-infección tuberculosa es una complicación común y debe investigarse en presencia de cualquiera masa gruesa a los rayos X.

2) La bronquiectasia de los lóbulos superiores es menos frecuentemente sintomática pero en otras partes del pulmón requiere tratamiento.

3) El tratamiento debe dirigirse primero hacia la reexpansión de la atelectasia que predispone a la bronquiectasia.

4) La lobectomía es el tratamiento de elección cuando hay síntomas y debe realizarse en los niños.

5) El término epituberculosis debe ser descartado como inadecuado para describir sombras que tienen varias significaciones patológicas y mecánicas.

6) El caracter serio de la bronquiectasia como complicación de la infección primaria tuberculosa da un peso mayor a la importancia de la profilaxis contra la tuberculosis especialmente entre los niños.

RESUME

1) La primo-infection tuberculeuse se complique communément de dilatation bronchique. Il faut la rechercher en présence de toute ombre radiologique massive.

2) La dilatation des bronches du lobe supérieur s'accompagne moins de manifestations cliniques, mais dans les autres parties du poumon, il y a lieu d'envisager un traitement.

3) Ce traitement doit d'abord être dirigé contre l'atélectasie qui prédispose à la dilatation des bronches.

4) La lobectomie est le traitement de choix quand la dilatation des bronches s'accompagne de manifestations cliniques et devrait être appliquée aux enfants.

5) Le terme d'épituberculose devrait être supprimé, car il ne rend pas compte des causes anatomiques et mécaniques variées qui sont à l'origine des ombres radiologiques.

6) La gramité des bronchiectasies que compliquent la primo-infection, donne un argument de plus à l'importance de la prophylaxie contre la tuberculose, plus particulièrement chez les enfants.

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Detection and Identification of Intracardiac Calcifications*

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Introduction

During the past 15 to 20 years the detection *in vivo* of intracardiac calcifications and their identification has become a fairly common accomplishment in the hands of careful, painstaking roentgenologists. No individual has contributed more toward stimulating his confreres in detecting these lesions than has Merrill Sosman, of Boston.[2,11,12] Among technical advances which have greatly aided in the visualization and identification of these lesions might be mentioned the more brilliantly fluorescent screens now commonly employed, the use of high-speed radiographic techniques (faster than 1/10 second), and the application of kymography. One must not fail at this point to emphasize the value of fluoroscopy both for detection and identification of many of these calcifications. The new Westinghouse fluoroscopic image amplifier or the Moon scanning tube, when perfected and available for general use by fluoroscopists, may render visible the more minute calcifications which are today revealed only with difficulty or not at all. I am, nevertheless, thoroughly convinced that to reduce the errors of omission and to aid in matters of differential diagnosis and exact localization, with present-day equipment, we do need high-speed, multiple, aimed, "spot" roentgenograms. Not only will calcification associated with coronary arteriosclerosis be much more frequently revealed, but occasionally other intracardiac calcifications, particularly the less marked degrees of valvular and annulus calcifications which cannot be visualized on roentgenoscopy, will be demonstrated. We have been using multiple, "spot," aimed, high-speed roentgenograms for study of the heart substance routinely for approximately five years, during which time the incidence of cases of calcification due to coronary arteriosclerosis exceeds that of valvular, myocardial, and pericardial calcifications combined. Our patients are for the most part of middle age or older. Many of those examined are highly intelligent private patients who want exact guidance as to their future physical and mental activities. Others are in the group who may

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be suffering both from occupational and non-occupational disease, and a most careful evaluation of all data obtainable is essential to the proper disposal of their claims before the Wisconsin State Industrial Commission. Our series includes approximately 100 cases of intracardiac calcification. We have as yet seen no case of calcified tumor nor any case of the endocardial calcification (excluding coronary atherosclerosis) which is said to occur occasionally on the endocardium opposite a septal defect, nor have we been certain of identifying calcification in the membranaceous septum[13] as may occasionally be demonstrated in patients with heart block.

Technique

All patients who are 40 years or older are carefully examined fluoroscopically with orthodiagraphy, and in addition to teleroentgenograms and esophagrams we take multiple, high-speed, aimed, "spot" roentgenograms on the same tunnel device permitting four exposures on a 10 x 12 film which many radiologists use for multiple radiographic study of the distal stomach and proximal duodenum or other portions of the gastrointestinal tract on certain occasions.[5] The important point of difference technically is that we change slightly the position of the patient for each "spot" film exposure, thereby aiding greatly in differentiating intra- from extracardiac calcifications. By means of this last-mentioned technical procedure applied routinely with small cone and short target-film distance (usually consisting of a single 10 x 12 roentgenogram with four exposures contained thereon) we have found an appre-

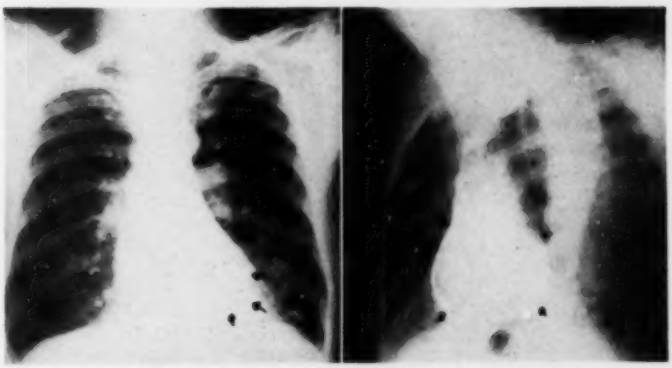

FIGURE 1: Pericardial calcification. Male, age 67, no recalled history of antecedent heart disease, no cardiac symptoms. Fluoroscopically shallow pulsations but no eras of absent pulsation. Rather characteristic limitation of pericardial calcification to ventricular surfaces.

ciably larger number of intracardiac calcifications, particularly coronary but also occasionally valvular calcifications, which would otherwise have been missed because of failure to visualize them with certainty fluoroscopically. I doubt not that radiologists differ in keenness of fluoroscopic vision, just as the keenness of perception may vary in a given individual from hour to hour or day to day, according to his physical fitness. We have for some time felt justified in placing chief reliance upon the multiple, high-speed, aimed, "spot" roentgenograms, aided occasionally by evidence obtained on kymography for the detection and identification of smaller intracardiac calcifications, just as many radiologists rely upon a series of routinely taken gastrointestinal or chest films to bring out the maximum diagnostic information regarding the more minute pathologies in these tracts which might otherwise be overlooked with roentgenoscopy alone or roentgenoscopy plus a minimum number of roentgenograms.

Significance

Concerning the significance of cardiac calcification, this may vary from the calcifications of the annulus fibrosus of the mitral or aortic valves which have no particular clinical importance, to ones in the valve leaflets or in the myocardium, which may contribute importantly to the diagnosis of chronic valvular heart disease[4] or previous myocardial infarction or pericarditis.[2] Coro-

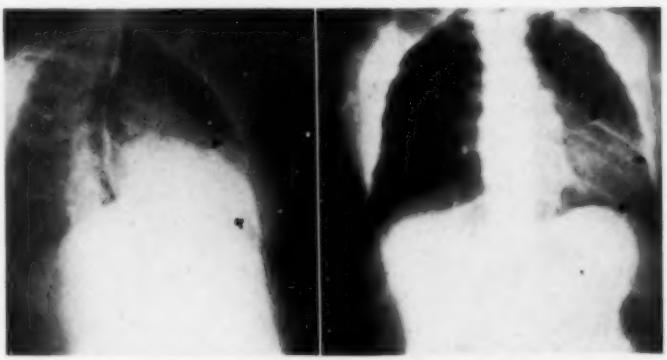

FIGURE 2 FIGURE 3

Figures 2 and 3: Calcified myocardial (anterior apical) infarct. Female, age 39, cardiac complaints, only four months' duration. Mild hypertension and mild heart failure clearing shortly prior to admission to hospital December 1, 1949. ECG confirmed presence of previous myocardial damage. No angina at time of attack or subsequent thereto. Bucky technique P.A. film reveals form of calcification better than non-Bucky films. Oblique shows characteristic distribution over anterior apical portion of left ventricle.

nary artery calcification per se may or may not be significant in relation to the patient's symptoms and medical history, and as stated by Sosman, "is to be reported as such." We may very properly add, however, that nearly all coronary arteriosclerosis is atherosclerosis and as such must be considered at least potentially dangerous, particularly when occurring in the earlier decades of life.

Incidence

The incidence of the various types of calcification would be influenced considerably by the age of the group studied. In a clinic or practice where upper age groups predominate, calcifications of the annulus fibrosus, the aortic valve, and the coronary arteries will occur with greater frequency than mitral valvular, myocardial, or pericardial calcifications. The youngest patient in whom the writer has seen calcification of the mitral valve was a male patient of 23 years whose past history for rheumatic infection was rather vague and inconclusive. The youngest patient with calcification seen in the aortic valve was a male of 39 years. A female, aged 39, was seen recently whose calcification was unquestionably myocardial. The youngest patient with well-defined coronary arteriosclerosis was a male, age 50.

Pericardial Calcification

Extensive pericardial calcifications in the personal experience of the writer have occurred more often than not as incidental findings and were apparently unassociated with any serious con-

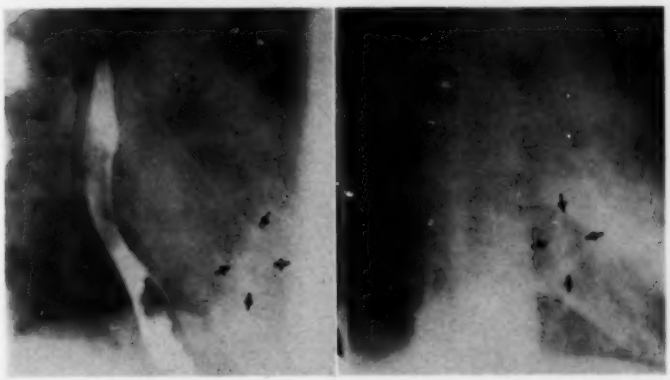

FIGURE 5: Mitral leaflet calcification. Male, age 24, recent hemoptysis, clinical suspicion auricular septal defect. P.A. and right oblique esophagrams show characteristic left auricular enlargement. Note low position of calcified mitral leaflets in relation to arc of esophageal compression.

strictive pericarditis phenomena. Several of these have been seen in individuals in the sixth or seventh decade who have enjoyed good health for many years and who have shown no signs of cardiac embarrassment or failure. One gave no history of previous pericarditis. The usual site of location is over the surfaces of the ventricles and as would be expected in the absence of any evidence of constrictive pericarditis clinically, these cases have shown fairly active excursions of the ventricular borders despite the encasement of the heart by large calcified placques (Figure 1). Sosman states that pericardial calcifications may be found as a ring along the auriculoventricular sulcus, or occasionally over the auricles.

Myocardial Calcification

Myocardial calcifications are of several types and etiologies, undoubtedly the most common being on the basis of an old massive myocardial infarction. The commonest location is the anterior apical portion of the left ventricle (Figures 2 and 3). We have seen two such cases, one recently, the other about 15 years ago (each with what might be described as a basket-weave type of calcification resembling somewhat a thick shell of a half egg when x-rayed in profile). The first was described by the internist reporting the case as resembling a "quarter moon." The one seen recently was found in a woman age 39, who had no history of previous coronary infarction, her cardiac history being based on symptoms going back a relatively short period of four months'

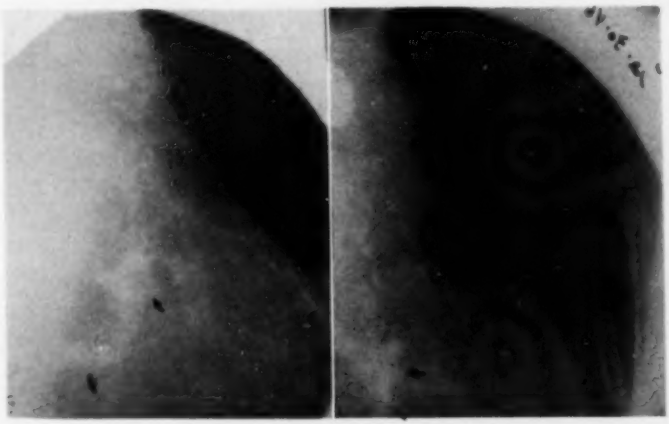

FIGURE 4: Mitral annulus calcification. Male, age 73, "four-on-one" 10 x 12 "spot," aimed, high speed radiographic exposures using tunnel technique. Wide excursion of annulus between systole and diastole shown well on two upper "spot" films of illustration.

time (Figures 2 and 3). Sepsis and calcium metastasis are also stated to be causes of calcification of the myocardium, but apparently the distribution in these pathologies is not of a type which would make them detectible roentgenographically.[1,3]

Valvular and Annulus Calcification

Probably in the experience of the average radiologist devoting only the usual amount of radiographic effort to the discovery of intracardiac calcification, this group would comprise his largest collection. Annulus calcifications of the mitral and less often the aortic ring are by no means rare in patients in the upper age groups and when being seen for the first time by the fluoroscopist afford considerable interest because of their large dancing excursions. The wide movement in *opposite* direction from the movement of the heart apex can be readily defined on careful analysis of the kymograms, as was pointed out by Rigler.[9] Also its wide excursion will frequently be radiographically revealed on our "four-on-one" multiple "spot" roentgenogram (Figure 4). Occasionally when the clinician is in doubt as to whether the chief cardiac lesion is a congenital or an acquired one (Figures 5, 6, 7 and 8) or when the clinical picture may not be clearly indicative of a valvular lesion, the x-ray detection of calcification of the aortic or mitral valve leaflets will add greatly toward the correct clinical evaluation.[4,7,11,12] Differentiation between annular and leaflet calcification is easier in the mitral area than in the aortic

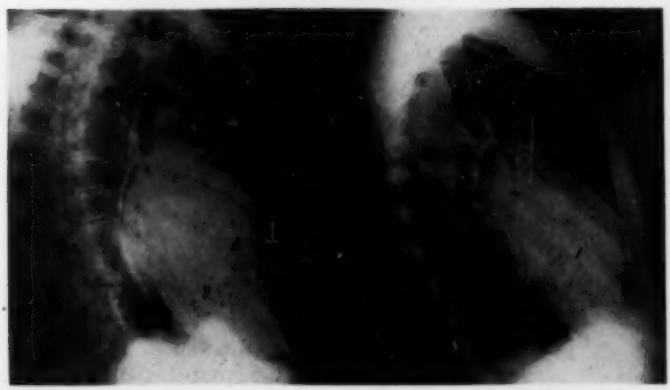

FIGURE 8: Mitral valve calcification. Right anterior oblique and left lateral teleroentgenograms adequately exposed (penetrated) to show intracardiac calcification of mitral leaflets. Note again the low posterior position of the valve during systolic phase. Characteristic esophagram findings again present. (Rarely, the esophagram may be normal). At post mortem some minimal calcification also present in aortic leaflets, not detected *in vivo*.

because the mitral valve ring calcification is actually somewhat less than a complete ring, being usually reversed-C or U-shaped. When a complete ring is formed or when there is a nodular thickening of calcareous deposits at the posterior branch of the calcified ring, as described recently by Windholz of Stanford,[13] one has radiologic evidence of extension of the calcification into the interventricular septum, this pathology being usually associated with heart block. The average age of patients having ring calcification is, of course, greater than those having leaflet calcification. However, the average age of patients with aortic calcification when detected *in vivo* is usually rather high, in contrast with which the mitral leaflet calcifications occur at a somewhat younger age.

As seen in postero-anterior study, aortic calcifications ordinarily are at a somewhat higher and more medial position than mitral calcifications. They are also in a somewhat more anterior position (Figures 9, 10, 11 and 12). However, these valves, it is to be emphasized, are anatomically not very widely separated, and differ-

FIGURE 9: Aortic valve calcification, female, age 64, known "leakage" for twenty years, left ventricle moderately enlarged. "U" form configuration revealed in "spot" roentgenogram lower left corner "four-on-one" roentgenogram. Formless configuration shown in upper right corner oblique projection.

entiation may at times be rather difficult, particularly if one does not have a frank aortic heart configuration or mitral heart configuration as a secondary aid. According to Sosman, if on the postero-anterior roentgenogram one draws an axis line obliquely

FIGURE 10: Same case as Figure 9. Position of valve rather high and anterior above auriculoventricular groove, shown on kymogram with patient in shallow left anterior oblique position.

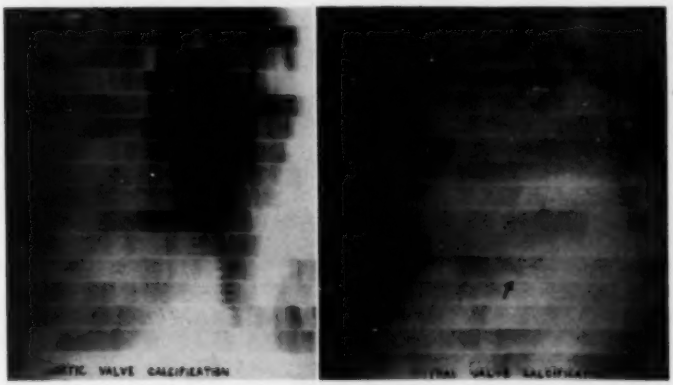

FIGURE 11: Left oblique kymograms, aortic valve and mitral valve calcifications, showing relatively similar position within cardiac outline when patient is examined in left oblique position. P.A. or rght anterior oblique study more helpful in differentiation of valve involved.

downward and to the right beginning at the auriculo-ventricular junction of the left heart border, both the mitral and aortic valves will lie in close relationship to this axis, the aortic being usually to the right and above it and the mitral to the left and below it. One should read, if interested, this article[12] in order to fully realize the wide area within which either the mitral or the aortic valve may lie (these two areas showing considerable "overlap"), in relation to the anterior chest wall when the heart is enlarged and deformed because of valvular disease. In calcified annulus cases the shadows are likely to be larger and denser and on the films more homogeneous than the mottled calcifications of the mitral or aortic leaflets. There is also said to be a slight difference in the character of the dancing excursion which the leaflets show as compared with the ring. It cannot be emphasized too strongly that routinely exposed teleroentgenograms will seldom reveal these abnormalities; careful search during fluoroscopy with complete dark room adaptation of the eyes, usually with the patient rotated into shallow right and left oblique positions, is necessary to "uncover" them; then the areas can be marked with a skin pencil applied to the posterior chest wall to indicate where the cone should be centered. Just as in "spotting" the patient for the "four-on-one" coronary study, so with the valvular calcifications the same radiographic technique may be used to great advantage in making detailed study of the character and movements of the densities. The kymogram is another means of studying and showing graphically for teaching purposes the nature of the ring and leaflet movements.[9]

Coronary Arteriosclerosis

That even marked degrees of coronary sclerosis may at times be present without clinical angina is well established by careful correlation of clinical history and post mortem studies of coronary pathology. This has prompted Sosman to say that "it indicates a specific type of damage in the specific case which can be reported only as such." Nevertheless, in a large series of 762 cases studied by Levy, Bruenn, and Kurtz, arteriosclerotic heart disease was the most frequent primary cause of death and cardiac insufficiency was the commonest terminal event. The importance of demonstrating and thus knowing the presence of coronary arteriosclerosis would be in inverse proportion to the age at which it was found. That is, it would be more significant if revealed in a patient age 50 than in one age 75 (Figure 14).

It is furthermore of interest to note that while coronary arteriosclerosis is very prevalent, it need not be accepted as inevitable that we all have it if we live to an advanced age. Ivy in a recent

discussion of drug therapy in degenerative diseases[6] quoting post mortem findings observed by Groddeck noted that 34 per cent of 283 persons of over 80 years of age had only slight sclerosis of the coronaries, while just 3 per cent of the group had only slight changes in the aorta. The youngest patient in our series of coronary arteriosclerosis was a male, age 50, who had had clinical angina pectoris for about one year (Figure 15). Considering distribution

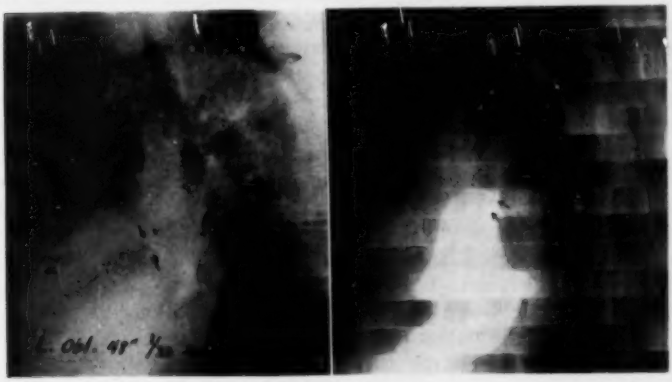

FIGURE 14: Left coronary arteriosclerosis. Male, age 59, end-on visualization of left coronary vessel with patient in left anterior oblique position, calcification visible fluoroscopically, also characteristically revealed in left oblique kymogram, which latter may reveal presence of lesser degrees of coronary sclerosis not visible on fluoroscopic study.

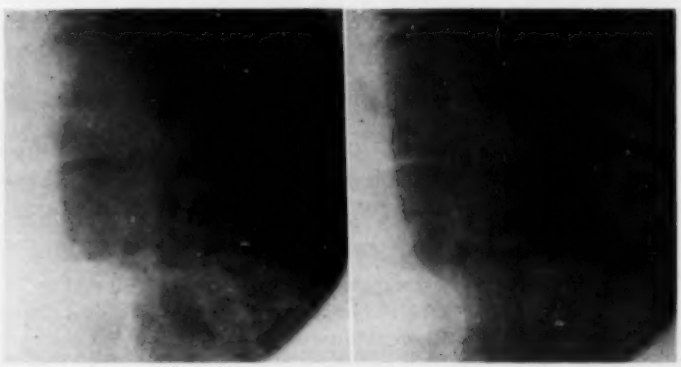

FIGURE 15: Left coronary arteriosclerosis. Male, age 50 (youngest case in our series of clearly definable coronary calcification). Rather characteristic angina for period of approximately one year. (From the amount of sclerosis present at time of x-ray study, one might reasonably conclude that this individual would have revealed x-ray evidence of the pathology at least a year or two earlier, had search been made at earlier date).

of sclerosis in a series of 34 cases studied by Saphir, Priest, Hamburger and Katz, "Sclerotic placques involving both the right and left arteries were found in 23 cases, in eight cases the left only was involved, and in two cases the right only."[10]

Concerning the relationship of sclerosis in the aorta and sclerosis in the coronary arteries, we have been able to demonstrate frank sclerotic placque formation in the coronary vessels in a number of instances where no placques could be demonstrated in the aortic arch. It behooves us, therefore, to make just as intensive search in the older age groups for coronary arteriosclerosis regardless of whether or not we have fluoroscopic or radiographic evidence of placque formations in the aortic arch.

Both on fluoroscopic examination and on multiple, aimed, "spot," high-speed roentgenograms we devote greater time and effort to the discovery of left coronary artery changes than right, for the two-fold reason of the greater incidence of more marked changes and because of their earlier occurrence in the left vessel and its branches. By varying the position of the patient slightly toward the right and left oblique positions for each of the four exposures on a 10 x 12 film, we can greatly facilitate the differentiation of coronary or other intracardiac calcifications from extracardiac calcifications, particularly calcified cartilages, bronchi, glands, or costovertebral articulations (Figure 13).

SUMMARY

The detection of intracardiac calcifications constitutes a fascinating study for the radiologist who is seeing cardiac patients in the older age groups and who has the time and interest to make adequate fluoroscopic and radiographic examination of each patient coming to him.

While the importance of roentgenoscopy cannot be overemphasized, multiple, aimed, "spot," high-speed roentgenograms will increase the incidence of detection and identification of these calcifications. A simple technical procedure for accomplishing this end result is described and recommended.

RESUMEN

El descubrimiento de las calcificaciones intracardiacas es un estudio muy atractivo para el radiólogo que ve enfermos cardiacos de edad avanzada y que tiene tiempo e interés para hacer exámenes adecuados fluoroscópicos y radiográficos en cada enfermo que a él viene.

Si bien la importancia de la radioscopia no puede jamás exagerarse, los roentgenogramas, múltiples, enfocados y localizados (spot) a alta velocidad, aumentan la frecuencia de los hallazgos

e identificación de esas calcificaciones. Un procedimiento técnico sencillo para obtener esto, se describe.

RESUME

La découverte des calcifications intracardiaques est extrêmement intéressante pour le radiologiste. Elle demande que l'examen soit fait avec précision, et sans hâte chez tous les malades âgés, qui viennent se fairë examiner radiologiquement le coeur.

Bien qu'on ne dira jamais assez l'importance de la radioscopie, les radiographies, faites nombreuses, bien dirigées, à très grande rapidité, augmenteront la fréquence de la découverte et de l'identification de ces calcifications. L'auteur décrit et recommande un procédé technique très simple qui permet d'obtenir ces résultats.

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Evaluation of Ioduron B in Bronchography

I. A Preliminary Study on Animal Tissues*

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The effects of a water soluble contrast medium (Ioduron B) upon tissues of the body have not been sufficiently investigated and reported in the literature. Fischer,[1] discussed briefly the effect of Ioduron B on the peritoneum of guinea pigs. A statement is also made that blood counts on patients subjected to Ioduron B bronchography show no material changes.

We have undertaken a more intensified and detailed study of the possible effects of this bronchographic medium, not only upon our patients but also upon test animals which have been subjected to Ioduron B bronchography.

The chemical evaluations on patients prior to and after bronchography have been reported in a separate paper.[2] Our results indicate slight transitory changes in chemical values shortly after bronchography with rapid return to normal values. Two of our patients and two of eight patients of Shefts,[3] complained of substernal pain immediately following bronchial instillation of Ioduron B and lasting for approximately 12 hours.

This paper is confined to evaluation of any morphologic changes in the tissues of test animals. Such changes, if present, combined with the previous chemical studies on humans, should offer conclusive evidence regarding the possible toxic effect of Ioduron B.

Materials and Methods Used:

Guinea pigs were utilized as the test animals. Each animal was anesthetized with ether and subjected to surgical exposure of the trachea, with injection of 0.3 cc. Ioduron B directly into the trachea and bronchial tree. The guinea pigs were anesthetized with ether. A midline incision was made over the trachea so it was exposed. A small 26 gauge needle was inserted into the trachea between the cartilaginous rings and the predetermined amount of Ioduron B was delivered from a tuberculin syringe. The syringe and needle

*Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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Ioduron B was supplied by "Wyeth, Incorporated, Philadelphia, Pa.

were then withdrawn and the wound closed. Three tenth cubic centimeters of Ioduron B in a 450 gram guinea pig was calculated to be the amount equivalent to 40 cc. in a 70 kilogram man. X-ray films taken shortly after direct instillation of the contrast medium demonstrate filling of the bronchial tree (Figures 1 and 2). Control animals were subjected to anesthesia without exposure of the trachea. Each animal was numbered and caged in pairs to avoid confusion and discrepancies in numbers.

Five groups of animals were studied. Each group consisted of four test and two control animals from the same litter. The total number of animals studied was 30, 10 of which constituted control animals. Group I consisted of test animals 1, 2, 3 and 5. These animals were sacrificed 48 hours after injection of Ioduron B into the bronchial tree. Control animals A and B were sacrificed 48 hours after anesthesia for comparison with the test animals. Group II consisted of test animals 6, 7, 8 and 9. These animals were sacrificed two weeks after administration of Ioduron B. Control animals C and D were sacrificed two weeks after anesthesia. Group III consisted of test animals 10, 11, 13 and 14. These animals were sacrificed three weeks after administration of Ioduron B. Control animals E and F were sacrificed three weeks after anesthesia. Group IV consisted of test animals 16, 19, 20 and 21. These animals were sacrificed six weeks after administration of Ioduron B. Control animals G and H were sacrificed six

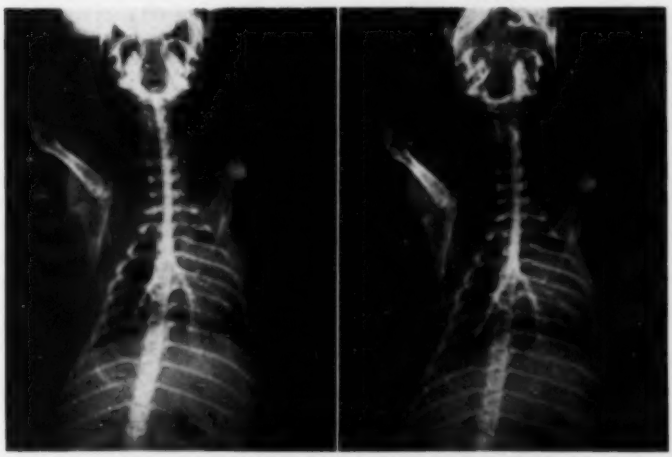

FIGURE 1 FIGURE 2

Figure 1: Roentgenogram of Guinea pig demonstrating Ioduron B in Bronchial tree.—*Figure 2:* Roentgenogram of Guinea pig demonstrating Ioduron B in Bronchial tree.

FIGURE 3

FIGURE 4

FIGURE 5

Figure 3: Photomicrograph demonstrating perivascular lymphocytic infiltrate of lung. (X170). — *Figure 4:* Photomicrograph demonstrating peribronchial lymphocytic infiltrate. (X170). — *Figure 5:* Photomicrograph demonstrating lymphocytic infiltrate in cortical zone of the kidney. (X170).

weeks after anesthesia. Group V consisted of test animals 22, 24, 25 and 26. These animals were sacrificed 12 weeks after administration of Ioduron B. Control animals I and J were sacrificed 12 weeks after anesthesia.

Inasmuch as the material was administered by means of the bronchial tree, absorbed by the blood, and excreted by the kidneys, it was deemed necessary to study microscopic sections of the following structures: (1) trachea, (2) both lungs, (3) heart, (4) liver, (5)both kidneys, (6) bladder. Each set of tissue studies was compared with those of the same group and tissues of all other groups. All changes were noted.

Guinea pigs 4, 17 and 18 died within 24 hours following intervention as a result of atelectasis, believed to be secondary to anesthesia. Guinea pig 23 died within 12 hours following surgical intervention as a result of exsanguination. Guinea pigs 12 and 15 died within two days following intervention. These animals showed evidences of having been attacked by other guinea pigs. The actual cause of death is not known, but pathologic studies of the tissues, grossly and microscopically, presented no variation from the normal.

Results

Group I: In these animals, microscopic examination of the lungs demonstrated a distinct perivascular (Figure 3) and peribronchial round cell infiltrate (Figure 4). The peritracheal lymph nodes showed slight hyperplasia. No other microscopic abnormality was noted in any other portion of the lungs. All other organs of the test animals were microscopically within normal limits. Sections from the two control animals did not present any features suggestive of a perivascular or peribronchial pulmonary infiltrate.

Group II: The lung sections showed complete disappearance of the perivascular and peribronchial round cell infiltrate. The tracheal lymph nodes were considered normal when compared with those of control animals. With the exception of the kidneys, all organs studied demonstrated no change over the control animals. Both kidneys of each test animal presented small, scattered, isolated foci of lymphocytes in the cortical zone (Figure 5). No such abnormality was noted in the control animals.

Groups III, IV and V: None of the organs presented any microscopic change when compared with control animals.

Discussion

Our preliminary investigation leads us to believe that Ioduron B, utilized as a new medium for bronchography, produces slight transitory tissue changes in test animals. The peribronchial and perivascular infiltrate seen 48 hours after instillation of Ioduron

B is explainable on a local reaction which probably takes place during transfer of the dye from the bronchial tree to the vascular system. This feature is transitory since it cannot be seen in sections of the lungs taken from test animals that have lived for two weeks or more. The renal involvement is also transitory and is probably caused by excretion of Ioduron B from the kidneys. This feature, although not present 48 hours after instillation of the dye, is seen within two weeks and then regresses to normal.

At present, test animals studied up to periods of 12 weeks following instillation of Ioduron B, show no evidence of permanent tissue damage or suggest the possibility of delayed toxic effects. We have a series of test animals which we will continue to study at frequent intervals until at least one year following instillation of this new water soluble bronchographic medium.

The deaths which occurred in this series could not be attributed to Ioduron B. In guinea pigs numbered 14, 17, 18 and 23, death was related to a known cause, unrelated to Ioduron B. However, in guinea pigs numbered 12 and 15, no actual cause of death was determined. It is possible that Ioduron B may have played some role, although we feel that this possibility is remote, since tissue studies revealed only normal findings.

Addendum: Our series of five test animals, which were permitted to live for one year following installation of Ioduron B, demonstrated no abnormal features either clinically or on microscopic examination of the vital organs.

SUMMARY

1) Ioduron B is not permanently damaging to tissues of test animals up to 12 weeks after intratracheal instillation of the dye.

2) Transitory inflammatory reactions are seen in the lungs and kidneys of test animals with complete disappearance within a short period of time.

RESUMEN

1) Ioduron B no daña permanentemente los tejidos de los animales en experiencia hasta 12 semanas después de la instilación intratraqueal del material.

2) En los pulmonaes y en los riñones de los animales de experiencia hay reacciones transitorias que desaparecen completamente dentro de corto tiempo.

RESUME

1) L'ioduron B ne cause pas de lésiones permanentes aux tissus d'animaux témoins observés douze semaines après instillation intratrachéale du produit.

2) Des réactions inflammatoires peuvent être observées au niveau des poumons et des reins des animaux témoins mais elles disparaissent complètement dans un court laps de temps.

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Evaluation of Ioduron B in Bronchography

II. A Preliminary Study in Man*

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Brandenstein,[1] recently reported a preliminary study on the use of Ioduron B for bronchography. This material was used on 25 patients with good radiologic contrast and no apparent adverse subjective symptomatology during a period of two months following bronchography. The solution is a water soluble radiopaque contrast medium which is rapidly absorbed by the blood from the bronchial tree, and apparently totally excreted by the kidneys (Figure 1). The physical properties of Ioduron B are as follows: Sp. gr. 1.29 at 20 degrees C., indefinitely stable at room temperature. At lower temperatures, the solution tends to crystallize, but will redissolve if warmed to 40 degrees C. for a period of 2 to 3 hours. The chemical formula is that of a diiodopyridon compound dissolved in the sodium salt of cellulose diycolic acid ether. The solution provides for increase in viscosity.

The development of Ioduron B and its mode of administration has been described by Fischer,[2] and by Brandenstein.[1] The problem with which this paper is concerned is not with the radiographic results following the use of Ioduron B, but rather the chemical evaluation of possible detrimental effects in man. Morphologic tissue studies in animals are being run concurrently and are reported separately.[3]

Methods and Materials:

Inasmuch as the material is water soluble and absorbed by the blood stream, the following series of laboratory studies were performed: complete blood count with hemoglobin determination, urinalysis, phenolsulphalein excretion test, blood urea nitrogen, blood cholesterol and esters, bromsulphalein, cephalin flocculation, and thymol turbidity. These tests were performed prior to bronchography as well as during the post-bronchographic period. Each patient was studied 24 to 48 hours prior to bronchography, 24 to

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Ioduron B was supplied by "Wyeth, Incorporated," Philadelphia, Pa.

48 hours after bronchography, and then at two week intervals for as long as five months in some cases. Two cases in which Iodochloral was used for bronchography were included in this study in order to essay a comparison between the two materials.

Discussion

Four patients (Tables II-V), showed a rise in cholesterol esters between two and four weeks after bronchography. It is significant that one of these patients (Table IV) also showed an elevation of esters one month after an esophagram which was done six weeks prior to bronchography. The significance of elevation of the cholesterol esters is not well understood. Most authors accept values between 40 and 60 per cent as normal variations. However, in view of the fact that four of the 10 patients studied in this group demonstrated elevations above the prebronchographic ester values at identical periods following bronchography, some change in liver function is suggested. One case (Table VI) showed a depression of the ester value four days after bronchography, the value returning to normal one month later. That this patient suffered some degree of temporary liver dysfunction seems apparent. One patient (Table VII) showed an abnormal elevation of thymol turbidity six weeks after bronchography. In one patient

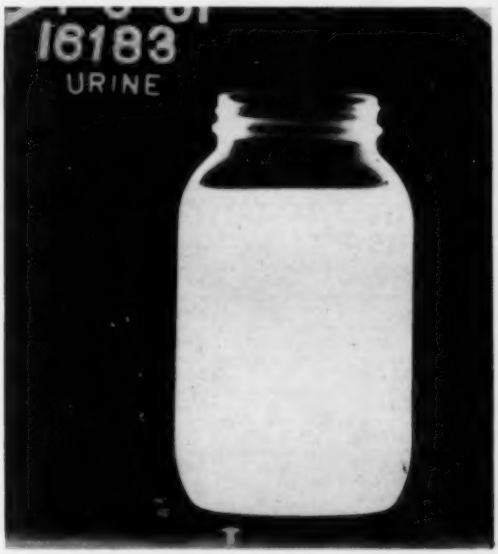

FIGURE 1: X-ray film of voided specimen.

(Table VIII) the BSP rose abnormally five weeks after bronchography. One patient (Table IV) showed a three plus cephalin flocculation one month after bronchography.

Of all patients showing changes in hepatic function, there were no changes that were not transitory. Furthermore, such changes that did occur were moderate.

TABLE II: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	8-7	8-15	8-18	8-24	9-8	10-25
RBC	5.5	*	5.0	5.4	5.75	5.2
WBC	7.4	*	8.0	7.9	9.0	5.9
HGB	120%	*	111%	110%	110%	101%
Urine	Neg.	*	Neg.	Neg.		Neg.
PSP	40%	*	45%	32%		40%
BUN	19.8	*	16.3	14.3	15.0	17
Cholesterol	233	*	196	227	214	221
Chol. Esters	38%	*	35%	50%	38%	
BSP	1.1%	*	4.0%	2.0%	2.0%	11%
Ceph. Flocc.	Neg.	*	Neg.	Neg.	Neg.	Neg.
Thym. Turbidity	3.0	*	1.0	4.0	6.7	5.4

* Rt. and Lt. Bronchogram 20 cc. and 10 cc. — Total 30 cc.

TABLE III: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	5-16	5-19	5-24	5-26	6-8	6-22	7-10
RBC	4.4		*	4.6	5.11	4.95	5.3
WBC	5.0		*	5.6	6.1	10.0	6.4
HGB	82%		*	90%	104%	87%	100%
Urine	Neg.		*	Neg.	Neg.	Neg.	
PSP		25%	*	45%		40%	45%
BUN	13.7		*	18.4		15.7	18.4
Cholesterol	352		*	372	333	352	
Chol. Esters	21%		*	31%	21%	51%	
BSP	Nor.		*	Nor.	Nor.	5.0%	3.0%
Ceph. Flocc.	Neg.		*	Neg.	Neg.	Neg.	Neg.
Thym. Turbidity	4.4		*	5.4	5.0	4.0	3.8

* Lt. Bronchogram 8 cc.

Two patients (Tables VI and VIII) showed a reduction in PSP excretion within 24 hours after bronchography. In each case, a corresponding rise in BUN occurred. One patient (Table IX), four days after bronchography, demonstrated a drop in PSP excretion without a corresponding rise in BUN. All patients demonstrated return to prebronchographic levels thereafter. In this small series,

TABLE IV: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	6-26	6-27	6-28	6-30	7-17	7-26	8-8	8-11	8-22	9-6
RBC	5.11		*	5.25	4.6	5.05	**	†	5.01	4.95
WBC	9.1		*	10.6	10.0	7.7	**	†	12.5	8.1
HGB	100%		*	100%	103%	103%	**	†	101%	100%
Urine	Neg.	Neg.	*		Neg.	Neg.	**	†	Neg.	Neg.
PSP	35%		*	75%	30%	30%	**	†		30%
BUN	17.7		*	19.1	18.4	18.4	**	†	14.3	15.7
Cholesterol	315		*	283	254	307	**	†	299	333
BSP	3.0%		*	2.0%	7.0%	3.0%	**	†	4.0%	1.0%
Ceph. Flocc.	Neg.		*	Neg.	Neg.	3+	**	†	Neg.	Neg.
Thym. Turbidity	7.6		*	2.2	2.2	5.0	**	†	6.0	5.8

* Esophagram 18 cc.
** Rt. and Lt. Bronchograms 40 cc.
† R.L.L. Bronchogram 17 cc.

TABLE V: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	6-7	6-13	6-15	6-29	7-6	8-2
RBC	5.2	*	4.7	4.5	5.4	4.5
WBC	7.8	*	10.6	7.5	8.3	6.3
HGB	105%	*	90%	90%	110%	90%
Urine	Neg.	*	Neg.			Neg.
PSP	35%	*	50%	75%		27%
BUN	22	*	21.3	17	19.1	19.8
Cholesterol	227	*	203	233		227
Chol. Esters	39%	*	37%	59%		45%
BSP	Nor.	*	Nor.	3.0%	1.0%	5.0%
Ceph. Flocc.	Neg.	*	Neg.	Neg.	Neg.	Neg.
Thym. Turbidity	1.6	*	1.0	2.0	2.0	1.0

* Rt. Bronchogram 20 cc.

TABLE VI: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	5-12	5-15	5-16	5-18	5-19	5-22	5-29	6-5	6-6	6-19	7-3
RBC		4.95		*	4.6			5.01		5.0	4.4
WBC		5.0		*	7.75			5.6		4.9	6.0
HGB		90%		*	86%			98%		100%	85%
Urine		Neg.		*	Neg.			Neg.		Neg.	Neg.
PSP	25%			*	15%				35%		30%
BUN		20.5		*	25.9		24.3	22.8		19.8	19.1
Cholesterol			240	*		275		279		268	240
Chol. Esters			65%	*		31%		39.7%		61%	
BSP		Nor.		*		Nor.		Nor.		7.0%	3.0%
Ceph. Flocc.			2+	*		2+		2+		Neg.	Neg.
Thym. Turbidity			11.2	*		12.6		9.0		10.4	8.0

* Rt. and Lt. Bronchograms 8 cc. each — Total 16 cc.

TABLE VII: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	5-16	5-19	5-23	5-24	5-24	5-26	6-8	6-20	6-22	7-10	8-9	10-24
RBC	4.75		*	5.1			5.19		4.8	5.10		
WBC	6.5		*	6.4	13.5		7.2		10.0	10.0		
HGB	93%		*	96%			106%		95%	95%		
Urine	Neg.		*	Neg.		Neg.	Neg.		Neg.			
PSP		25%	*		35%				20%	20%		
BUN	19.1		*	26.8		25.1		21.3	23.5	25.1		22.0
Cholesterol	207		*	299			21.3		268			247
Chol. Esters	22%		*		37%		41%		47%			35%
BSP	Nor.		*		Nor.		Nor.		7.0	6.0	3.0	6.5
Ceph. Flocc.	14		*		1+		Neg.		1+	Neg.	Neg.	
Thym. Turbidity	2.6		*		4.4		5.4		6.0	12.2	8.6	4.0

* Rt. and Lt. Bronchograms 18 cc.

30 per cent of the patients showed this significant although transitory renal function deterioration.

In one patient (Table VI), the cephalin-flocculation and thymol turbidity were abnormal before and after bronchography. No further marked change in function occurred for a period almost

TABLE VIII: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	6-27	6-29	6-30	7-14	8-2	8-17	8-31
RBC	5.25	*	5.2	5.3	5.2	5.0	5.3
WBC	6.5	*	9.0	7.8	7.0	5.8	7.3
HGB	105%	*	95%	106%	113%	110%	115%
Urine	Neg.	*	Neg.	Neg.	Neg.	Neg.	
PSP	45%	*	25%	80%	30%	100%	23%
BUN	19.8	*	25.1	18.2	17.7	17.0	14.3
Cholesterol	383	*	283	275	333	333	299
Chol. Esters	51%	*	58%	50%	40%	34%	46%
BSP	7.0%	*	7.0%	7.5%	11.0%	3.0%	2.0%
Ceph. Flocc.	2+	*	Neg.	Neg.	Neg.	Neg.	1+
Thym. Turbidity	2.2	*	6.0	2.0	3.0	2.0	4.0

* Rt. Bronchogram 20 cc.

TABLE IX: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	5-16	5-17	5-17	5-19	5-22	5-23	5-31	6-28
RBC		4.85	*	**	4.80		†	4.9
WBC		7.7	*	**	11.6		†	14.6
HGB		90%	*	**	84%		†	90%
Urine		Neg.	*	**	Neg.		†	Neg.
PSP	40%		*	**		20%	†	40%
BUN		18.4	*	**	15	15.7	†	20.5
Cholesterol	227		*	**		185	†	268
Chol. Esters	54%		*	**		59.4%	†	42%
BSP	Nor.		*	**	Nor.		†	2.0%
Ceph. Flocc.	Neg.		*	**		Neg.	†	Neg.
Thym. Turbidity	2.6		*	**		2.0	†	1.2

* Esophagram 51 cc.
** Bronchogram 15 cc.
† Rt. Bronchogram 10 cc.

two months following the use of Ioduron B. However, transitory changes did occur as noted previously.

In summary, six patients showed some change in hepatic function. Two patients of the 10 studied showed changes both in renal and hepatic function. In all, seven patients, or 70 per cent, showed either hepatic or renal function changes, or both. Nevertheless,

TABLE X: RESULTS OBTAINED IN PATIENT FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	6-7	6-9	6-12	6-22	6-27	7-10	7-27	8-25	9-7
RBC	5.0	*	4.8	4.1	**	4.95	4.95	4.8	4.5
WBC	5.7	*	6.4	6.5	**	5.2	6.5	9.0	7.0
HGB	90%	*	95%	84%	**	95%	95%	91%	85%
Urine	Neg.	*	Neg.	Neg.	**		Neg.	Neg.	Neg.
PSP	30%	*	40%	30%	**	25%	30%	35%	40%
BUN	20.5	*	17	15.7	**	19.8	17.7	15.7	17.7
Cholesterol	215	*	283	333	**		247	237	268
Chol. Esters	60%	*	67%	52%	**		51%	52%	51%
BSP	Nor.	*	Nor.	5%	**	5.0%	5.5%	5.5%	3.0%
Ceph. Flocc.	Neg.	*	Neg.	Neg.	**	Neg.	Neg.	Neg.	Neg.
Thym. Turbidity	3.8	*	3.4	2.6	**	3.0	1.0	4.0	3.4

* Esophagram.
** Esophagram 24 cc.

TABLE XI: RESULTS OBTAINED IN PATIENTS FOLLOWING IODURON B BRONCHOGRAPHY

All Dates are in the year 1950

	7-28	8-7	8-9
RBC	5.30	*	5.10
WBC	11.5	*	9.1
HGB	105%	*	95%
Urine	Neg.	*	Neg.
PSP		*	35%
BUN	22.0	*	19.8
Cholesterol	247	*	315
Chol. Esters	61%	*	37%
BSP	2%	*	7.5%
Ceph. Flocc.	3+	*	3+
Thym. Turbidity		*	9.4

* Lt. Bronchogram 20 cc.

all changes were transitory and left no apparent permanent effects in patients.

In a previous publication,[3] we have demonstrated that transitory pulmonary and renal inflammatory reactions occur in guinea pigs two weeks following intra-tracheal instillation of Ioduron B. It is reasonable to assume that the same pathologic effect occurs

TABLE XII: RESULTS OBTAINED FOLLOWING LIPIODOL BRONCHOGRAPHY

All Dates are in the year 1950

	6-15	6-20	6-22	7-7	7-21	8-28	8-31
RBC	4.75	*	4.75	5.12	4.75		
WBC	7.0	*	7.4	7.1	5.0		
HGB	90	*	80	104	95		
Urine	Neg.	*	Neg.	Neg.		Neg.	
PSP	45%	*		40%		10%	38%
BUN	18.4	*	16.3	17.7		14.3	
Cholesterol	221	*	208		254	261	
Chol. Esters	48%	*	40%		55%	57%	
BSP	Nor.	*	11.0%	3.0%	4.0%	4.5%	
Ceph. Flocc.	1+	*	Neg.	Neg.	Neg.	Neg.	
Thym. Turbidity	3.4	*	4.0	3.0	3.8	2.2	

* Rt. and Lt. Bronchograms.

TABLE XIII: RESULTS OBTAINED FOLLOWING LIPIODOL BRONCHOGRAPHY

All Dates are in the year 1950

	6-7	6-16	6-18	7-3	7-17	7-27
RBC	5.1	*		4.75	5.0	5.15
WBC	9.3	*		7.2	7.8	10.1
HGB	106%	*		95%	95%	106%
Urine	Neg.	*		Neg.	Neg.	Neg.
PSP	35%	*	45%	20%	45%	80%
BUN	23.5	*	18.4	20.5	19.1	15.7
Cholesterol	308	*	324	352	240	240
Chol. Esters	38%	*	55%		38%	60%
BSP	Nor.	*	4.0%	3.0%	3.0%	1.0%
Ceph. Flocc.	Neg.	*	Neg.	Neg.	Neg.	Neg.
Thym. Turbidity	5.8	*	3.8	5.4	4.0	3.0

* Rt. and Lt. Bronchograms.

in man, particularly in view of the mild transitory renal function changes occurring in three of the 10 patients in this group.

On the basis of these results, we feel that the work should be continued. The use of Ioduron B, at least at the present, should be carefully controlled. As yet, the possibility still exists that some of the effects we have noted in this very small group of patients, may well prove permanent in a larger series. Perhaps, if these patients are followed for a longer period, permanent changes may appear. Thus far, there is no reason to suppose that this new contrast medium is more toxic than lipiodol and similar substances now in wide use. This, together with certain advantages pointed out by Brandenstein,[1] warrant the continuation of this study.

SUMMARY

1) Hepatic function changes occur in 60 per cent of patients in whom Ioduron B is used for bronchography. The changes may occur within a few hours to as long as six weeks following bronchography. These changes are transitory.

2) Renal function changes occur in 30 per cent of patients. The changes occur within a few hours or a few days following the use of Ioduron B. These changes are transitory.

3) Both hepatic and renal transitory changes occurred in 20 per cent of the patients.

4) Either hepatic or renal transitory changes, or both, occurred in 70 per cent of the patients.

5) The results obtained are sufficient to warrant further investigation, since all functional impairment encountered was of a mild nature and quite transitory as far as could be determined.

RESUMEN

1) En el 60 por ciento de los enfermos en quienes se usa Ioduron B hay alteraciones de la función hepatica, cuando se usa el producto en broncografía. Los cambios pueden ocurrir ya sea dentro de pocas horas o hasta seis semanas después de la broncografía. Estas alteraciones son transitorias.

2) Hay alteraciones renales en el 30 por ciento de los enfermos. Estas ocurren dentro de pocas horas o pocos días después del uso del Iodurón B. Estos cambios son transitorios.

3) Ambas alteraciones, la renal y la hepática ocurren en el 20 por ciento de los enfermos.

4) Una u otra de las alteraciones renal o hepática ocurrieron en el 70 por ciento de los enfermos.

5) Los resultados obtenidos son suficientes para justificar una investigación ulterior puesto que todas las alteraciones fueron moderadas y transitorias hasta donde se pudo conocer.

RESUME

1) Des altérations de la fonction hépatique se produisirent chez 60% des malades chez lesquels fut pratiquée une bronchographie à l'aide de l'ioduron B. Ces altérations peuvent se produire quelques heures après la bronchographie, et peuvent se maintenir jusqu'à six semaines après. Ces altérations sont transitoires.

2) Des altérations de la fonction rénale peuvent survenir chez 30% des malades. Elles se constituent en l'espace de quelques heures ou de quelques jours. Ces altérations sont transitoires.

3) Chez 20% des malades, on à constaté l'atteinte simultanée du foie et du rein.

4) Des altérations hépatiques ou rénales transitoires, ou des altérations frappant les deux viscères à la fois ont été notées chez 70% des malades.

5) Les résultats obtenus justifient des investigations ultérieures. Il s'agit en effet dans tous les cas d'atteintes légères et transitoires.

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Lung Immobilization Chamber Therapy in Chronic Pulmonary Tuberculosis*

(With Case Reports)

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Introduction

During recent years methods of promoting rest and relaxation of the diseased lung in pulmonary tuberculosis have been suggested and developed for clinical use. Decrease in the functional activity of tuberculous lungs is still considered a most important factor in the clearing of inflammatory exudates and the closure of cavities, being of equal, or even greater importance than chemotherapy.

It is the purpose of this paper to report the results of four years trial of immobilizing lung chamber therapy in chronic pulmonary tuberculosis, to discuss critera for the selection of patients for this form of therapy, and to attempt to evaluate its place in the overall treatment program.

Methods

The method by which local rest of the lungs is achieved and the mechanism by which adequate pulmonary ventilation is provided in the use of the lung immobilizing chamber has been discussed in detail by Barach and co-workers.[1-3] The patient lies in an enclosed chamber† in which air can be alternately compressed and decompressed at differential pressures of 55 to 60 mms. of mercury and at a rate of 25 to 30 times a minute, resulting in a tidal flow of 300 to 500 ml. of air in and out of the lungs. The body compartment of the chamber is separated from the head end by a movable partition which lowers over the neck to produce differential pressures between 4 and 12 cm. of water in the head compartment. The addition of this pressure to the compression (positive) cycle of air as it enters the head compartment is adequate to overcome the resistance of the tracheobronchial tree, thus allowing equal air pressure to be simultaneously applied to the inner and outer surfaces of the chest wall as well as the upper and lower surfaces of the diaphragm. The immobilizing chamber

*From the District No. 1 Tuberculosis Sanatorium, Decatur, Alabama.
†Manufactured by J. H. Emerson Company, Cambridge, Massachusetts.

is air conditioned. The head compartment is equipped with a two-way communication device. A light for reading and a small battery radio may be placed beside the head. By means of a release catch the patient may enter and leave the chamber without help. There are three such chambers in operation at our institution. With our present plan of treatment, each machine is operated on two shifts of 10 hours each; thus enabling six patients to be undergoing treatment during a given period (usually four to six months). By proper training, most patients learn to immobilize their chest wall and diaphragm in the first week of practice, thereafter the chest is immobilized without conscious or voluntary effort. With an occasional patient claustrophobia is a deterrent to complete immobilization; in others, nervousness and inability to relax prohibit lung immobilization. Recently we have found Tolserol* to be very helpful in promoting muscular relaxation and in shortening the training period.

Results

Clinical reports of other investigators have shown that lung immobilization therapy with the equalizing pressure chamber has been effective in the closure of cavities and the arrest of disease in moderately and far advanced pulmonary tuberculosis.[1-7]

During the past four years we have used this form of therapy in 23 patients, eight of whom could not cooperate in learning or maintaining lung immobilization; the treatment of these cases was terminated after a trial period of from four to eight weeks. Fifteen patients immobilized well and were treated for periods sufficiently long for adequate evaluation. Five of these 15 patients were considered failures in regard to this form of therapy.

Of the remaining 10 patients, four were arrested as a result of immobilizing lung chamber therapy alone, four were arrested with chemotherapy used in conjunction, and in two patients disease on one side was arrested enabling thoracoplasty to be performed on the opposite side.

Since the number of cases treated is by necessity too small for statistical analysis, each case must be considered on its own merits. The case histories of the 10 patients successfully treated will be presented.

Case Reports

Case 1: L.E.M., a white male, 20 years of age, was first admitted to the sanatorium August 31, 1945, with a diagnosis of far advanced pulmonary tuberculosis. Because of cavity formation in the right upper lobe, right therapeutic pneumothorax was instituted but could not be maintained.

*Supplied through the courtesy of H. Sidney Newcomer, M.D., E. R. Squibb and Sons, New York City.

FIGURE 1a FIGURE 1b FIGURE 1c

CASE 1, L.E.M.

Figure 1a: X-ray film May 18, 1947, at the beginning of lung immobilizing therapy. Note cavities in right first and second anterior interspaces.—*Figure 1b:* X-ray film July 22, 1947, after two months therapy.—*Figure 1c:* X-ray film March 24, 1950, two and one-half years after therapy showing only fibrotic infiltration in the right lung field.

A cross-spread occurred to the left side and left therapeutic pneumothorax was instituted October 8, 1945, and abandoned four months later. A left phreniclasis was performed and shortly thereafter he was discharged unimproved. He was re-admitted six months later, July 28, 1946, because of left tuberculous empyema and during the next 10 months received periodic aspirations. Repeated sputum examinations remained positive for tubercle bacilli. X-ray examinations during this interval showed extensive tuberculous infiltration with multiple cavities in the right upper lobe and pleural thickening on the left side with diminishing amounts of fluid and re-expansion of the lung. On May 18, 1947, the patient began lung immobilization therapy with the equalizing pressure chamber. X-ray film of the lungs at that time is shown in Figure 1a. He was kept in the chamber four hours daily for four months. Sputum examinations were negative after the first month in the machine. The patient's cough, which was productive of eight to 10 cups of sputum daily, had become non-productive and infrequent. An x-ray film of the lungs taken July 22, 1947 (Figure 1b), two months after institution of this therapy showed the cavities in the right upper lobe to be lost to view. After two more months of immobilization therapy, he was discharged to be followed in the out-patient clinic.

A recent x-ray film of the lungs, March 24, 1950 (Figure 1c), revealed only fibrotic infiltration in the right upper lobe and left pleural thickening.

Comment: Case 1 was the first patient treated by lung immobilization in our institution. It is noteworthy that although he was kept in the immobilizer only four hours a day, resolution of the far advanced disease was remarkably rapid.

Case 2: M.K., a white male, 30 years of age, was admitted to the sanatorium August 11, 1946, with the diagnosis of moderately advanced pulmonary tuberculosis. X-ray films revealed extensive tuberculous infiltration in both upper lung fields. A cavity was present in the right first anterior interspace and there were multiple cavities in the left upper lung field. Sputum examinations were consistently positive. Left therapeutic pneumothorax was instituted August 19, 1946, and was continued until March, 1947, when it had to be abandoned. Right therapeutic pneumothorax was begun October 21, 1946, and was abandoned one month later because of dense adhesions. One gram of streptomycin was given daily from August, 1947 to May, 1948, with very little improvement. Pneumoperitoneum was tried from January, 1948 to May, 1948, without appreciable improvement. He was maintained on bed rest alone until December 9, 1949, when he was placed in the lung immobilizer 10 hours per day for a period of six months. At the beginning of chamber therapy, x-ray film of the lungs (Figure 2a) showed a cavity still present in the right first anterior interspace and multiple cavities present in the left upper lung field. Sputum examinations were positive. After six months of immobilization therapy, tomograms of the right lung at the 10 cm. level revealed fibrotic infiltration with closure of the cavity (Figure 2b). Since the left side disease had remained essentially unchanged left upper stage thoracoplasty was performed in August, 1950. Follow-up x-ray film (Figure 2c) revealed a successful left thoracoplasty with fibrosis in the right apex and first anterior interspace. He has been seen at regular

FIGURE 2a

FIGURE 2b

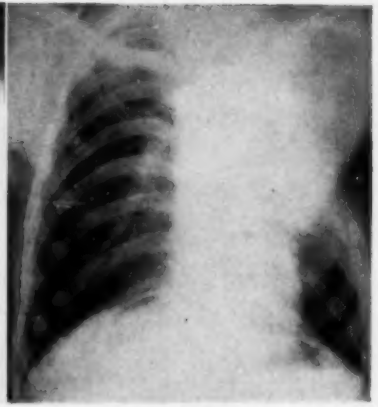

FIGURE 2c

CASE 2. M.K.

Figure 2a: X-ray film at the beginning of chamber therapy. Note cavity in right first anterior interspace and "honeycombing" in left upper lung field.—*Figure 2b:* Tomogram of right lung showing absence of cavity after six months of immobilization therapy.—*Figure 2c:* X-ray after left upper stage thoracoplasty. Clinical arrest of bilateral disease.

intervals since and has remained well. Repeated sputum examinations from September, 1950, to date have been negative.

Case 3: L.K., a white female, age 20, was admitted to the sanatorium April 11, 1949. She had a history of progressive far advanced tuberculosis of two years duration. She had been given pneumoperitoneum therapy

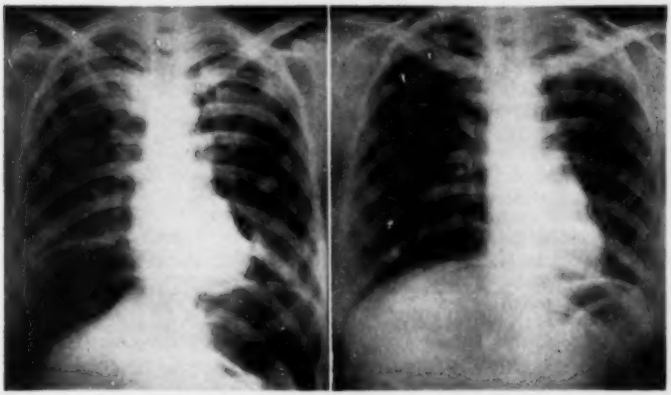

FIGURE 3a FIGURE 3b

CASE 3, L.K.

Figure 3a: X-ray film before chamber therapy. Note giant cavities in both upper lung fields.—*Figure 3b:* X-ray film after six months of immobilization therapy. Note that the cavity on the right is lost to view. The cavity on the left is still present.

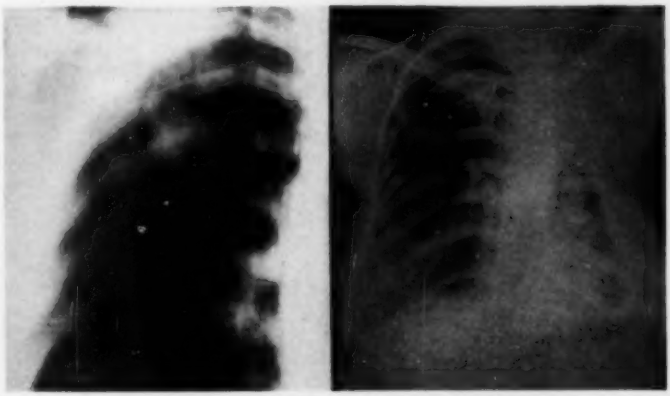

FIGURE 3c FIGURE 3d

CASE 3, L.K.

Figure 3c: Tomogram of the right lung giving confirmation of cavity closure.
Figure 3d: X-ray film after left upper stage thoracoplasty. Clinical arrest of bilateral far advanced disease.

for the previous year in another sanatorium and discharged with maximum hospital benefit. X-ray film of the lungs (Figure 3a) revealed extensive tuberculous infiltration and giant cavities in both upper lobes. Repeated sputum examinations were positive for tubercle bacilli. The sedimentation rate (Cutler method) was 26 mm. in one hour. Both right and left artificial pneumothorax were attempted, without success. Pneumoperitoneum was re-instituted. Para aminosalicylic acid was given for five months and she was kept at bed rest. There was no significant improvement. On January 15, 1950, she began lung immobilization therapy in the equalizing pressure chamber 10 hours per day. After six months of chamber therapy an x-ray film of the lungs (Figure 3b) showed the cavity in the right apex to be lost to view. A tomogram (Figure 3c) confirmed this. In July, 1950, after a preparatory course of streptomycin, left upper stage thoracoplasty was performed (Figure 3d). She underwent a six months period of convalescence and during this time repeated sputum examinations were negative. She has remained well to date.

Comment: Cases 2 and 3 exemplify the important part lung immobilization therapy can play in the preparation of the ordinarily hopeless case for surgery. In both cases the disease was bi-lateral, cavitary and far advanced. With six months of immobilization therapy, the disease on one side was arrested sufficiently that a successful thoracoplasty could be performed on the opposite side. Case 2 had a great variety of therapeutic measures including 10 months of streptomycin therapy with very little benefit. Case 3 had received bed rest, pneumoperitoneum and a five months course of para aminosalicylic acid before immobilization therapy was begun.

Case 4: O.S., a white nurse, 38 years of age, was admitted to this sanatorium October 6, 1940. Diagnosis of pulmonary tuberculosis had been made six years previously and 18 months of bed rest had resulted in apparent stability of the tuberculous infiltration present in the upper third of both lungs. Shortly before admission a cavity appeared in the left upper lung field. Bed rest and left therapeutic pneumothorax were instituted. In July, 1942, a left extrapleural pneumothorax was performed since the intrapleural pneumothorax had become impossible to maintain because of dense adhesions. The extrapleural pneumothorax was maintained with air until August, 1947, after which the lung was allowed to re-expand. In July, 1947, cavitation appeared in the right first interspace and sputum examinations for tubercle bacilli were positive. X-ray film of the lungs July 22, 1947 (Figure 4a) showed the left extrapleural pneumothorax and tuberculous infiltration in the upper third of the right lung with cavitation in the right first anterior interspace. There was diffuse pulmonary fibrosis throughout both lung fields, which mitigated against another surgical procedure. Beginning in August, 1947, the patient was given immobilization therapy four hours daily for a period of six months. During the last two months of this therapy, one gram of streptomycin was given daily. There was no appreciable improvement. During this time the patient had difficulty in immobilizing due to claustrophobia. This was gradually overcome. She was then placed in the chamber eight hours daily for five months and immobilization was satis-

factory. Streptomycin was continued during this period. An x-ray film taken May 27, 1948 (Figure 4b) at the end of immobilization therapy showed disappearance of the cavities on the right and marked resolution of the tuberculous infiltration. Sputum examinations were consistently negative for tubercle bacilli. She has remained well and is working full time.

Case 5: L.C.T., a white male, 24 years of age, was discovered to have pulmonary tuberculosis January 18, 1950 (Figure 5a). He was placed at strict bed rest at home. On February 26, 1950, he was admitted to this sanatorium because of apparent lack of improvement. X-ray film inspection of the lungs (Figure 5b) revealed a cavity approximately 3½ cm. in diameter in the right first anterior interspace which had definitely increased in size since the first examination. Sputum examinations for tubercle bacilli were consistently positive. Sedimentation rate (Cutler method) was 17 mm. in one hour. Right therapeutic pneumothorax was instituted, but had to be abandoned after a few days. On March 13, 1950, he began lung immobilization therapy in the equalizing pressure chamber 10 hours daily. On May 17, 1950, an x-ray film of the lungs (Figure 5c) showed the cavity to be lost to view. All sputum examinations were negative. The sedimentation rate became normal. Weekly fluoroscopic examination during this time showed progressive improvement. He was kept at bed rest for six weeks following immobilization therapy and was discharged July 7, 1950. He had received one gram of streptomycin every other day and 12 grams of para aminosalicylic acid daily from April 13, 1950, until discharge. Since discharge the patient has been followed in the out-patient clinic and has remained well to date.

Case 6: W.W.G., a white female, 33 years of age, was admitted to this sanatorium October 17, 1949, with the diagnosis of moderately advanced pulmonary tuberculosis. She had been under treatment in another state

FIGURE 4a FIGURE 4b

CASE 4, O.S.

Figure 4a: X-ray film July 22, 1947, before beginning immobilizing therapy. Note cavity in right first anterior interspace, inner zone.—*Figure 4b:* X-ray film May 27, 1948, after second period of lung immobilizing therapy showing cavity lost to view.

FIGURE 5a FIGURE 5b FIGURE 5c

CASE 5, L.C.T.

Figure 5a: Initial diagnostic x-ray film January 18, 1950. Note cavity beneath right first anterior rib, mid-zone region. — *Figure 5b:* X-ray film February 28, 1950, after one month of strict bed rest. Note increase in size of cavity.—*Figure 5c:* X-ray film May 17, 1950, after two months of immobilization therapy. Cavity lost to view.

three years previously and discharged apparently arrested. Admission x-ray film (Figure 6a) revealed thickening of the pleura bi-laterally and slight fibrotic infiltration in the upper third of the left lung with a cavity measuring 3 x 2 cm. in diameter present in the outer zone of the second anterior interspace. Repeated sputum examinations were positive. Sedimentation rate (Cutler method) was 23 mm. in one hour. She began lung immobilization therapy shortly after admission, remaining in the chamber 10 hours daily for three months. She received one gram streptomycin daily and para aminosalicylic acid 12 grams daily from October 18, 1949 to January 20, 1950. On January 16, 1950, an x-ray film (Figure 6b) showed the cavity to be lost to view. All sputum examinations had become negative. There was a weight gain of 20 pounds. Since discharge from the sanatorium January 20, 1950, she has been followed through her family physician and has remained well to date.

Case 7: G.H., a white female, 25 years of age, was found to have pulmonary tuberculosis August 18, 1950 (Figure 7a). She was admitted to the sanatorium October 1, 1950, having been treated with strict bed rest at home during the interval prior to admission. During this time her disease advanced considerably and admission x-ray film (Figure 7b) revealed exudative and productive infiltration in the upper third of both lung fields, with a large cavity 5 cm. in diameter located in the first and second anterior interspaces. Sputum examinations were repeatedly positive. Sedimentation rate (Cutler method) was 26 mm. in one hour. The patient began lung immobilization therapy October 3, 1950, remaining in the chamber 10 hours daily for five months. She also received 12 grams of para aminosalicylic acid daily. Tolserol elixir® was given to promote lung immobilization and general relaxation, 1 gram being given 30 minutes before entering the chamber, 1 gram after five hours immo-

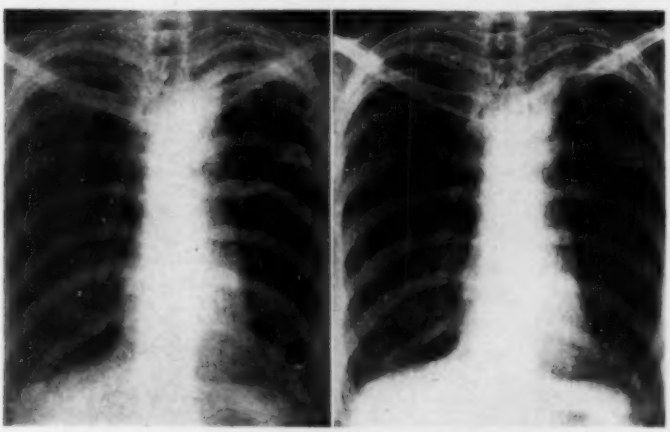

FIGURE 6a FIGURE 6b

CASE 6, W.W.G.

Figure 6a: X-ray film October 27, 1949, before beginning immobilization therapy. Note cavity in left third anterior interspace, outer zone.—*Figure 6b:* X-ray film January 16, 1950, after 12 weeks therapy. Cavity lost to view.

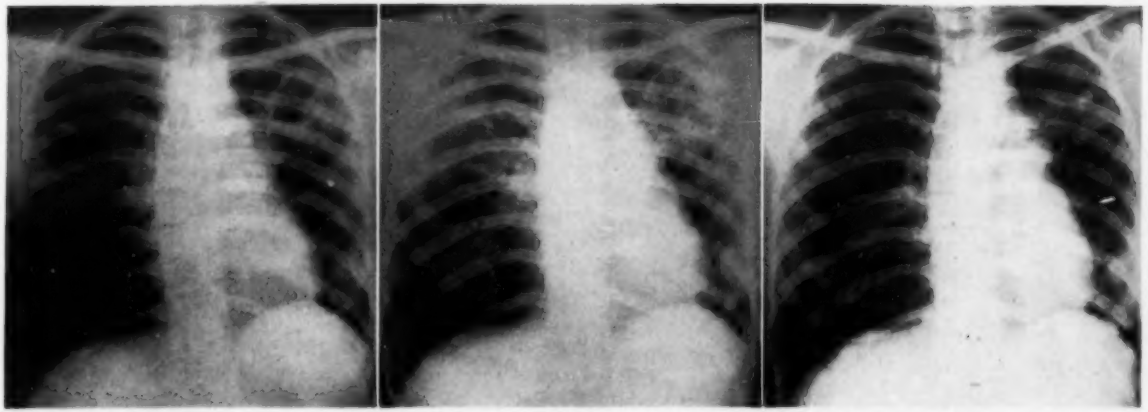

FIGURE 7a FIGURE 7b FIGURE 7c

CASE 7, G.H.

Figure 7a: Survey x-ray film August 18, 1950. Note large cavity in the left first and second anterior interspaces.—*Figure 7b: X-ray* film October 2, 1950, at the beginning of lung immobilizing therapy and after six weeks of strict bed rest. Note great increase in size of the cavity.—*Figure 7c:* X-ray film January 2, 1951, after three months therapy. Cavity lost to view. Confirmed by fluoroscopy.

bilization and 1 gram at the end of the 10 hour period. Weekly fluoroscopic examinations showed progressive improvement in the disease with diminution in the size of the cavity. In January, 1951, an x-ray film (Figure 7c) showed the cavity to be lost to view. Lung immobilization therapy was continued until February 23, 1951, and 1 gram of streptomycin was given every third day in an attempt to stabilize the healing process.

Comment: Cases 4, 5, 6 and 7 are examples of moderately and far advanced cavitary disease in which chemotherapy was employed in conjunction with lung immobilization. Case 4 was the second patient treated in the chamber at our hospital. Because of her poor prognosis she was given streptomycin disregarding its possible effect on the evaluation of lung immobilization therapy. However, the first two months of streptomycin therapy produced no visible improvement, furthermore, it has been our experience that streptomycin only rarely is effective in the closure of large cavities of long standing. In rare instances, streptomycin appears responsible for the closure of tension cavities by its effect on the attendant bronchial lesions. Case 7 had far advanced disease. Para aminosalicylic acid was given for the first four months of the chamber therapy and streptomycin given concurrently during the last month of therapy. We now feel that chemotherapy judiciously employed is a logical and helpful procedure during the period of lung immobilization and in no way minimizes the importance of pressure chamber therapy. Cases 5 and 6 were treated in this manner with excellent results.

Case 8: R.B., a white male veteran, age 28, was admitted to the sanatorium June 12, 1950, with a history of non-productive cough, mild fever, loss of weight and strength over a period of two months. An x-ray film of the chest made during a survey revealed a small cavity in the left apex. Two weeks prior to admission, he experienced pleuritic pain in his left chest. Admission x-ray examination (Figure 8a) revealed exudative and productive tuberculous infiltration in the left apex with a cavity measuring 3 x 3 cm. There was a small pleural effusion in the base. Sputum examinations were positive for tubercle bacilli. Sedimentation rate (Cutler method) was 19 mm. in one hour. He was placed at strict bed rest; no specific medication was given. At the end of one month an x-ray film (Figure 8b) showed clearing of the pleural effusion and of the exudative infiltration in the left apex, but the cavity had increased in diameter. He then began lung immobilization therapy, remaining in the chamber 10 hours daily for two months. At the end of this time upon fluoroscopic examination and roentgenogram (Figure 8c) the cavity was lost to view. He had gained in weight and strength. Repeated sputum examinations were negative. He has remained well to date.

Case 9: R.E.P., a white male, age 43, was first admitted to the sanatorium February 7, 1949, complaining of cough, expectoration, night sweats, loss of weight, and indigestion. Tuberculous infiltration was

*E. R. Squibb and Sons.

FIGURE 8a FIGURE 8b FIGURE 8c

CASE 8, R.B.

Figure 8a: X-ray film June 13, 1950. Note cavity in left first and second anterior interspaces, outer zone. — *Figure 8b:* X-ray film July 14, 1950, at the beginning of immobilization therapy and after one month of strict bed rest. Note clearing of pleural effusion but increase in size of the cavity.—*Figure 8c:* X-ray film September 14, 1950, after two months of lung immobilizing therapy. Cavity lost to view.

present in the upper third of the right lung field with a small cavity in the right first anterior interspace and tuberculous infiltration without evident cavitation was present in the left upper lung field. Sputum examinations were positive for tubercle bacilli. The sedimentation rate (Cutler method) was 20 mm. in one hour. The disease was known to have been present at least a year prior to this admission. The patient refused collapse therapy. He was given streptomycin, one gram daily, and Promizole, two grams daily, for three months. An x-ray film May, 1949, showed definite improvement. Sputum examinations were negative. On May 9, 1949, he left the hospital against medical advice. He was re-admitted May 22, 1950, and an x-ray film of the lungs (Figure 9a) revealed tuberculous infiltration in both upper thirds with a small cavity in the right apex and a larger cavity, 3 x 2 cm., beneath the second anterior rib. Sputum examinations were positive for tubercle bacilli. He was placed at bed rest and amithiozone in dosage of 75 milligrams daily was given. After one month of this regimen, there was no evident improvement. He was then placed in the lung immobilizing chamber, 10 hours daily for two months. X-ray film (Figure 9b) then showed both cavities lost to view and residual fibrosis in the upper third of each lung field. Sputum examinations were negative for tubercle bacilli and he was discharged August 24, 1950. He has remained well to date.

Case 10: C.G., a white male, 20 years of age, was discovered to have pulmonary tuberculosis in January, 1950 (Figure 10a). There was tuberculous infiltration in the right first and second anterior interspaces with a cavity measuring 1½ x 2 cm. in the second right interspace. Sputum examinations were positive. Under the supervision of his family doctor, the patient was placed at strict bed rest for one month. No specific medication was given. Because of apparent lack of improvement he was admitted to the sanatorium February 21, 1950. An x-ray film (Figure 10b) revealed enlargement of the cavity. Repeated sputum ex-

FIGURE 9a FIGURE 9b

CASE 9, R.E.P.

Figure 9a: X-ray film before lung immobilizing therapy. Note cavity in left first anterior interspace.—*Figure 9b:* X-ray film after two months therapy showing cavity lost to view.

FIGURE 10a FIGURE 10b FIGURE 10c

CASE 10, C.G.

Figure 10a: X-ray film January 3, 1950, showing cavity in the right second anterior interspace.—*Figure 10b:* X-ray film February 21, 1950, after strict bed rest. Note increase in size of cavity.—*Figure 10c:* X-ray film May 17, 1950 after three months lung immobilization therapy. Cavity lost to view.

aminations were positive for tubercle bacilli. His symptoms were those of cough, expectoration and low-grade fever. The sedimentation rate (Cutler method) was 20 mm. in one hour. He was then given lung immobilization therapy 10 hours daily for three months. No antibiotic was given. At the end of two months therapy, sputum examinations were negative and upon fluoroscopy the cavity was lost to view. His sedimentation rate had become 5 mm. in one hour. An x-ray film (Figure 10c) taken at the end of three months showed the cavity to have disappeared and only residual fibrotic infiltration in its place. He was discharged July 7, 1950, to be followed in the out-patient clinic and has remained well to this date.

Comment: Cases 8, 9 and 10 above have in common that the cavities increased in size upon bed rest, disappeared after two months therapy with lung immobilization and the fact that chemotherapy was not given during the period of chamber treatment. The results of these cases suggest that chamber therapy be extended to patients with earlier and less extensive cavitary disease obviating some of the well known disadvantages and complications of usual methods of collapse therapy.

Discussion

Since the number of patients that can be treated in a given period is small, the careful selection of patients for lung immobilization therapy is important. Otherwise all concerned become discouraged at the repeated failures. In this study failures were classed as initial or treatment failures.

Initial Failures: In our experience extremely nervous and restless individuals undergoing much mental turmoil cannot immobilize properly or remain in the machine for sufficiently long periods of time. The use of mephenesin (Tolserol* used in this study) has enabled us to successfully treat some cases of this type. We have learned to avoid individuals with psychopathic personalities who cannot follow any type of treatment long or who do not have the will or the desire to become well. Patients who have claustrophobia, as a rule, do poorly. Others who reside in the machine during the 10 hour period at night are unable to adjust themselves to sleeping in daytime. In some patients who then sleep in the machine, chest movement may take place.

Individuals with sinus and middle ear disease frequently suffer much discomfort and may have exacerbations which resist all treatment. In our experience, such measures as vaso-constrictor sprays or nose drops, antibiotics, ear plugs and sponge ear pads help this class of patients very little. Most of them must discontinue immobilization therapy.

One or more of the above factors were responsible for the initial

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failure of the eight patients in our series who could not learn or maintain lung immobilization. At the present time most patients of this type are not considered for this form of therapy.

Treatment Failures: The main conditions within the chest which seem to be responsible for treatment failures are extensive fibrosis with rigid thick walled cavities of long standing and marked pleural thickening as may occur from previous artificial pneumothorax. These factors appeared responsible for the failure in at least three of the five patients who had long periods of adequate lung immobilization. However some of the cases successfully arrested and reported above had extensive fibrosis, therefore it is not always possible to determine with certainty whether such cases should be denied lung immobilizing therapy.

There are several factors to be considered in evaluating the place of lung immobilization chamber therapy in the overall treatment program of pulmonary tuberculosis. Expense is one such factor, allowing the use of only a few machines in the average institution devoted to care of the tuberculous. Since a patient must reside in the chamber at least 10 hours a day for a period of four to six months in order to achieve good results, it can be seen that few patients can be treated in the course of one year. However, there are certain advantages of this form of therapy as it concerns the individual patient. Both lungs are rested simultaneously. There are no complicating structural changes in the lung or pleura as a result of this therapy, consequently, there is no corresponding loss of pulmonary function. By utilizing the lung immobilizing chamber for a relatively short period of time, a patient with moderately advanced disease may be saved many months of treatment with other types of collapse therapy which result in loss of pulmonary function. We feel that lung immobilizing therapy should have a definite place in the treatment of those patients whose cavities are increasing in size upon bed rest, in those with bilateral cavities particularly when such cavities are unaccompanied by marked fibrous tissue reaction, and in certain patients as a preparation for "salvage surgery". Since lung immobilizing therapy is considered to be only an exaggerated form of lung rest, chemotherapy may be used in conjunction according to the same indications and contraindications as when combined with ordinary bed rest.

In evaluating lung rest as a therapeutic agent for cavitary tuberculosis, the effectiveness with which the method is employed warrants a brief comment. In our judgement the use of a semicontinuous 10 hour treatment, either during the day or night, is superior to shorter periods with longer intervals between chamber therapy. Furthermore, the patient should be kept at strict bed

rest when out of the chamber, and vigorous chest examinations and maximal breathing tests, which may tend toward cavity inflation, avoided.

SUMMARY

1) The results in 23 cases treated by lung immobilizing chamber therapy in our institution over a period of the past four years are described. Eight of these were considered initial failures in patients who were unable to learn or maintain correct lung immobilization. Five of the 23 cases were treatment failures, in which arrest was not achieved after long periods of adequate lung immobilization. The 10 remaining patients were clinically arrested in whole or in part due to lung immobilizing chamber therapy and have remained well for periods ranging from six to 42 months.

2) The case histories of 10 patients in whom arrest of disease took place are reported with illustrative roentgenographic pictures.

3) The limitations and advantages of lung immobilizing therapy are discussed. Careful selection of patients is emphasized.

4) The use of the lung immobilizing chamber is stressed as an adjunct to the therapy of chronic pulmonary tuberculosis which is of value in the closure of cavities and arrest of disease without resulting in loss of pulmonary function.

RESUMEN

1) Se describen los resultados obtenidos en 23 casos tratados por medio de la cámara de inmovilización en nuestra institución por un período de cuatro años. Ocho de estos casos fueron considerados al principio como fracasos, por tratarse de enfermos incapaces de aprender a mantener la inmovilización correcta. Cinco de los 23 casos tratados lo fueron sin éxito, en los que no se logró detención de la enfermedad después de largos períodos de inmovilización. Los restantes 10 fueron considerados clínicamente como detenidos en parte o completamente a causa del tratamiento en la cámara de inmovilización, y han permanecido bien por períodos de 6 a 42 meses.

2) Se presentan las historias clínicas de 10 enfermos en los que la enfermedad se logró detener, y se muestran radiografías ilustrativas.

3) Se discuten las limitaciones y las ventajas de la inmovilización del pulmón. Se llama la atención sobre la cuidadosa selección de los enfermos.

4) El uso de la cámara de inmovilización se recomienda como adjunto al tratamiento de la tuberculosis pulmonar, que se de valor en la clausura de excavaciones y la detención de la enfermedad, sin pérdida de la función pulmonar.

RESUME

1) Les auteurs donnent les résultats de 23 cas traités par la chambre d'immobilisation puemonaire pendant ces quatre dernières années. Huit d'entre eux ont été considérés comme des échecs, il s'agissait de malades qui furent incapables de s'astreindre à une immobilisation pulmonaire correcte ou qui ne la supportèrent pas assez longtemps. Cinq sont des échecs du traitement: malgré une longue période d'immobilisation correcte, il n'y entre pas d'arrêt de l'évolution. Les dix malades restants furent cliniquement stabilisés en partie ou totalement grâce à la chambre d'immobilisation pulmonaire; ils sont demeurés en bonne santé pendant un laps de temps de six à quarante deux mois.

2) Les auteurs rapportent l'histoire clinique des dix malades qui furent stabilisés avec les images radiographiques.

3) Ils discutent les limites et les avantages du traitement par immobilisation pulmonaire et insistent sur le soin que l'on doit apporter au choix des malades.

4) Ils mettent l'accent sur le rôle de la chambre d'immobilisation pulmonaire comme traitement adjuvant de la tuberculose pulmonaire chronique. Ils montrent sa valeur dans la fermeture des cavernes et l'arrêt de l'évolution, sans aucune action fâcheuse sur la fonction pulmonaire.

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Pathogenesis of So-called Idiopathic Spontaneous Pneumothorax and Related Conditions*

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Since the research work of Fischer-Wasels by anatomic methods, we know that in the pathogenesis of so-called idiopathic spontaneous pneumothorax certain bullae, situated on the surface of the lung, play an important part. Later our concept was further extended by pleural endoscopy which made possible not only exact diagnosis, but also effective therapy. We learned by means of biopsy that the bullae can be small or large, even gigantic, usually multiple, but sometimes isolated, particularly the large kind. The bullae are by no means limited to the apex; they may also be found on the whole surface of the lung. The bulla arising from a cicatrized region is a very frequent phenomenon but not necessarily so.

According to general opinion the beginning of spontaneous pneumothorax based on bullae, comes from the rupture of a bulla. This has been proved by anatomy, endoscopy and by operation. There can, therefore, be no doubt concerning this mechanism of the origin of spontaneous pneumothorax. There also can be no doubt that another mechanism exists, that is the permeability of a bulla—without rupture, and without collapse of the latter. In 1940 I established in a monograph,† concerning spontaneous pneumothorax, that a bulla with a very attenuated wall is able to produce and maintain chronic pneumothorax without any previous rupture.

This conclusion was founded on observation with the endoscope. Before the operation it had been determined by the intrapleural pressure that the air had not ceased to escape from the lung. Endoscopy showed one solitary bulla of a gigantic size, originating in the inferior lobe of the right lung with greatly attenuated walls and in a state of tension. This was treated successfully by local irritation of the bulla.

The hypothesis of passage of air through the visceral pleura which has become thin, without macroscopic lesion is not without analogies. Sohmincke in 1924 describes a case in which he supposed the pleura to be permeable because of defective develop-

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†"Der idiopathische Spontanpneumothorax und ahuliche Krankheitsbilder," *Erp. inn. Med. Kinderhk.*, 59:213-283.

ment. Lately Brock, based on operative results, described a "porous pleura."

Recently I have observed two cases, following closely on each other, which by clinical and biopsy findings proved the permeability of certain bullae.

Case 1: Sch., aged 30. There was a question of a tuberculous infiltration of the left lung. Artificial pneumothorax was established and completed on November 25, 1949, by a Jacobaeus operation. At the end of the operation one solitary bulla of the size of a chestnut was visible in the inner part of the apex of the totally collapsed lung. When leaving the hospital, the attention of the patient was drawn to the possibility of spontaneous pneumothorax. On January 17, at 11 p.m. the expected accident took place, while the patient was in bed. She felt a sudden oppression on the left side. Next day a control proved a slight increase of the intrapleural pressure and a pronounced collapse. Some exsufflations relieved the patient but only temporarily. For this reason endoscopy was done on February 16, 1950. We were surprised to find the bulla in its whole size tender and protruding but with no adhesions or other remarkable change. After local irritation of the bulla and repetition of this procedure, the intrapleural pressure and collapse of the lung became normal.

Case 2: This is the case of a woman R. M., aged 49. At the age of 20 she suffered from apicitis and in 1939 of spontaneous pneumothorax of the right side for three weeks. At the beginning of 1949 she had a recurrence on the same side. The pneumothorax was benign, not very large, and circular with moderately elevated pressure.

In the right apex were a few cicatrices of no great importance. In the right eye was a chronic iritis supposed to be specific. After six weeks of irritation therapy the lung reexpanded. In April 1950, the third attack occurred. She was sitting in an armchair and suddenly felt pain on the right side followed by a feeling of oppression.

This time the pneumothorax was larger and the intrapleural pressure was above zero. The x-ray film revealed evidence of quite thin adhesions. On April 27, 1950, it was surprising to see a nearly infinite number of thread-like adhesions which suspended the superior lobe. Below the apex on the anterior surface of the lung there was a solitary bulla the size of a prune, very taut and fixed by a group of adhesions in the cupula of the pleura. After section of the adhesions the bulla remained taut and its shape did not change. Half an hour later, when the total section was concluded, a renewed inspection of the bulla showed that it had distended but not collapsed and that it was in a lower position. Next day the intrapleural pressure was negative, two months later there was complete re-expansion of the lung. What is certain in this case is, that there was no gaping fistula held open by fixing adhesions, as is usually presumed in medical literature and which occurs sometimes if there is a torn bulla. Here the bulla was macroscopically intact, it remained tightly stretched immediately after section and only at the end of the operation it had distended but not collapsed.

I conclude from this that it was a permeable bulla. The adhesions acted as a valvular mechanism in the bronchioles belonging to the bulla. After their section the mechanism of the valve was

abolished and the pressure in the interior of the bulla corresponded again to the pressure in the interior of the lung. This is why air ceased to escape through the permeable bulla.

SUMMARY

There exists two forms of so-called idiopathic spontaneous pneumothorax. One is very benign and due to a sub-pleural bulla which has become permeable. The intrapleural pressure is moderately increased; the volume of air escaping through the bulla is small. Soon an equilibrium is established between the pressure of the bulla and that of the pleural cavity which limits the outgoing air. The part played by the adhesions consists of favoring the genesis and the swelling of the bulla. It is the nature of this benign form that there is never any pleural effusion or hemothorax. Evacuation of air gives real relief and continual drainage is not necessary. In these chronic or recurring cases pleural irritation appears indicated, and in cases of adhesions, their section.

The beginning of pneumothorax of this kind does not necessarily depend upon a mechanical factor. The moment when the bulla becomes permeable depends on the degree of attenuation or thinness of the wall.

Exceptionally the clinical situation is a dramatic one in case of bilateral pneumothorax, in the presence of serious lesions of the lung, of myocardial disease, or of aged patients. At necropsy, the pathologist endeavors in vain to find a torn bulla as I have witnessed many times.

The clinical picture of the second form of spontaneous pneumothorax is due to a ruptured bulla or laceration of pulmonary tissue, which is usually serious. Pressure is considerably increased and the lung greatly collapsed, while the mediastinum is deviated. Aspiration of air has a palliative effect since the volume of air coming from the bronchioles without the intermediary of a tightly stretched bulla is of importance. In order to save the patient's life, one must in some cases establish a continual drainage. The part played by adhesions is important in the pathogenesis of rupture of bullae and other lacerations. The starting of pneumothorax by physical effort or trauma is significant. Hemothorax or pleural effusion can occur because of the lesion of the lung and of the direct communication of the bronchial tree with the pleural cavity.

RESUMEN

Existen dos formas del llamado neumotórax espontáneo idiopático. Una es muy benigna y es debida a una bula subpleural que

se hace permeable. La presión intrapleural es moderadamente aumentada; el volumen de aire que escapa a través de la bula es pequeño. Pronto se establece el equilibrio entre la presión de la bula y la del espacio pleural, lo que limita la salida de aire. El papel desempañado por las adherencias consiste en que favorece la génesis y la infliación de la bula. En estos casos nunca hay derrame pleural o hemotórax. La exacuación del aire produce alivio y el drenaje continuo no es necesario. En estos casos crónicos o recurrentes la irritación pleural parece indicada y en casos de adherencias está indicada su sección.

El principio del neumotórax de esta clase no depende necesariamente de un factor mecánico. El momento en que la bula se perfora depende del grado de adelgazamiento de la pared de ella.

Excepcional la situación clínica es dramática en caso de neumotórax bilateral en presencia de serias lesiones del pulmón, de afecciones del miocardio o en personas de edad avanzada. En la necropsia el patólogo trata en vano de encontrar la bula desgarrada como lo he presenciado muchas veces.

El cuadro clínico del segundo tipo de neumotórax espontáneo se debe a una bula rota o laceración del tejido pulmonar que generalmente es seria. La presión aumenta considerablemente y el pulmón muy colapsado y el mediastino desviado. La aspiración de aire tiene efecto paliativo puesto que el volumen de aire viniendo de los bronquiolos sin interposición de una bula distendida es de importancia. Para salvar la vida del enfermo se debe establecer el drenaje continuo. La importancia de las adherencias es grande en la patogenia de la ruptura de la bula y en otras laceraciones. El inicio del neumotórax por un esfuerzo o trauma es significativo. El hemotórax o el derrame pleural pueden ocurrir a causa de la lesión pulmonar y por la directa comunicación del arbol bronquial con la pleura.

RESUME

Il y a deux catégories du pneumothorax spontané et idiopathiques. L'une est très bénigne, elle est due au fait qu'une bulle souspleurale est devenue perméable à l'air qu'elle contient. La pression intra-pleurale est modérément augmentée, l'air qui s'échappé de la bulle est d'un volume réduit. Vite s'établit un équilibre entre la pression de la bulle et la pression de la cavité pleurale, et cet équilibre limite l'issue de l'air. Les adhérences jouent un rôle en favorisant la création de la bulle et son gonflement. Dans ces formes bénignes, il n'y a jamais épanchement pleural ou hémothorax. La simple évacuation de l'air donne une guérison véritable, et il est inutile de mettre le malade en drainage continue. Dans

les cas chroniques ou récidivants, l'irritation pleurale est indiquée. S'il y a des adhérences, elles doivent être sectionnées.

La création d'un pneumothorax de cette catégorie ne dépend pas nécessairement d'un facteur mécanique. La bulle devient perméable au moment où se constitue une diminution suffisante de l'épaisseur de sa paroi.

Exceptionnellement la situation est dramatique. Il s'agit alors de pneumothorax bilatéral, de lésions pulmonaires importantes, d'atteinte myocardique, ou de malades âgés. A l'autopsie, les constatations anatomo-pathologiques ne permettent pas de mettre en évidence la déchirure de la bulle.

Dans le second type de pneumothorax spontané, le tableau clinique est généralement sérieux. Il est en rapport avec une rupture de bulle ou une dilacération du poumon. La pression augmente considérablement, le poumon est violemment collabé, le médiastin est dévié. L'aspiration de l'air a un effet palliatif. Elle cesse d'agir quand le volume de l'air venant directement des bronches devient important. Il faut dans certains cas, pour sauver la vie du malade, mettre en oeuvre un drainage continu. Le rôle joué par les adhérences est important dans l'origine de la rupture des bulles et des autres lésions. Il est significatif de constater qu'un pneumothorax peut se constituer après un effort physique ou un traumatisme. Un hémothorax ou un épanchement pleural peut survenir. Ces complications sont dues à la lésion du poumon et à la communication directe de l'arbre bronchique dans la cavité pleurale.

Bronchial Onset of Reinfection Tuberculosis in the Adult*

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During 1948 and 1949, and the first four months of 1950, we made x-ray examinations of chests and bronchial lavages in 500 persons intimately living with patients carrying tubercle bacilli, previously registered in the Furbush Dispensary.

This collective or mass examination was made for research purposes, that is, to study the existence of tuberculosis in these human groups, indiscriminately, regardless of the stage of disease or symptoms. This examination showed 20 per cent tuberculous lesions suspected by x-ray films, and confirmed by finding tubercle bacilli in bronchial washings. In fact bronchial lavage revealed tubercle bacilli in 36 per cent and x-ray examination showed evidence of disease in only 20 per cent. This disparity compelled us to bronchoscope all persons showing acid-fast bacilli in bronchial lavage. We bronchoscoped 95 of these cases with positive bronchial lavage, and we found 40 per cent with tracheobronchial lesions, of which 24 per cent showed lesions in the radiography and 16 per cent did not show lesions in the radiography. These cases ranged from 17 to 35 years of age.

The 14 cases with tracheo-bronchial lesion, with positive bronchial lavage and normal radiography, constitutes the essential purpose of the present work. A careful examination of these patients, most of them with normal radiography for over two years previous to this investigation, allows us to affirm that we have discovered a new syndrome, composed of tracheobronchial tuberculous lesions in the adult, in the first stage of the disease.

This new bronchial tuberculous syndrome discovered before the disease has invaded the lung is, in our judgment, a way tuberculosis begins in the adult, which is different from those cases in which it starts in the pleura or in the lungs. Therefore, we have to give all of them the same importance and emphasize that tuberculosis may first appear in the pleura, parenchyma, or the bronchi. When establishing an early diagnosis of tuberculosis, the methods used should include bronchial lavage and bronchoscopy, especially in persons living with tuberculous patients.

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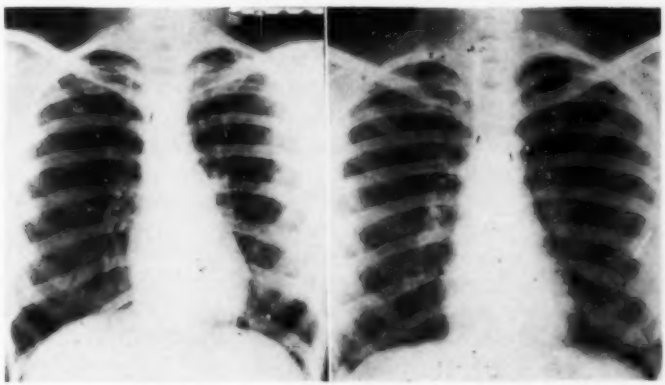
*Presented at the First International Congress on Diseases of the Chest, Rome, Italy, September 21, 1950.

We maintain that the 14 cases of tracheo-bronchial tuberculosis discovered are early lesions in these adults who have repeatedly been reactors to tuberculin.

The serial radiographic study of these cases allow us to affirm that no demonstrable parenchymatous lesions have existed and, therefore, bronchial lesions are not subsequent to the same, nor are they a sequel or vestige of controlled pulmonary lesions. They evidently are beginning lesions appearing previous to any demonstrable pulmonary tuberculosis. These are not cases of *solitary bronchial tuberculosis*, as those described by professors Soulas, Capó, Meyer and many others. Similarly, Dr. Juan Carlos Dighiero, Uruguay, presented at the Sixth Panamerican Congress of Tuberculosis, in Havana, January 1945, a study entitled "Forms of Initiation of Tracheo-Bronchial Tuberculosis in the Adult" in which he presented cases of solitary bronchial tuberculosis. None of the above authors discovered lesions in the early stage of the disease



CASE 1 CASE 2

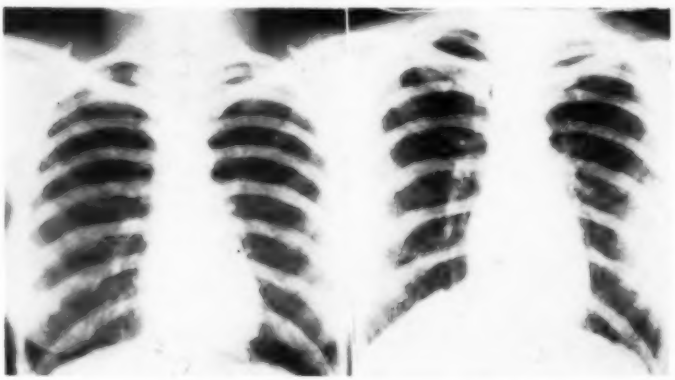
Case 1: Beginning Bronchial Tuberculosis Case—Superficial Infiltroulcerating Form, with Positive Bronchial Lavage and no Lesions in the Radiography. Eighteen year old female has intimately lived with her contagious sister for a year. Tuberculin reaction was negative, and she was completely asymptomatic. X-ray film shows no pulmonary lesion. Bronchial lavage revealed tubercle bacilli. Bronchoscopy showed superficial infiltroulcerative lesions, at the inlet of the bronchus in the right upper lobe and at the inlet of the main bronchus of same side.

Case 2: Beginning Bronchial Tuberculosis Case—Infiltroulcerous Form and Positive Bronchial Lavage Cured with Several Applications of 10 per cent Silver Nitrate. Twenty-two year old single, white male, lived with his mother, a contagious case of tuberculosis, for two years. He reacted to tuberculin but was completely asymptomatic. Bronchial lavage showed tubercle bacilli. Radiography does not reveal any significant pulmonary lesion. Bronchoscopy presents an infiltroulcerative lesion in the main left bronchus. After four bronchoscopic treatments with 10 per cent silver nitrate, the lesion was apparently cured, and further bronchial lavage did not reveal tubercle bacilli.

as we have done, that is, with no clinic symptoms or positive sputum. Our cases did not come to us but rather we went to them through radiography, bronchial lavage, and bronchoscopy, making these discoveries through pure investigation or suspicion.

Moreover, we have followed for two years some of these cases with x-ray films, without finding any disease in the lungs, but maintaining their lesions in a tracheal or bronchial location, remaining asymptomatic. Some cases have been cured with several applications of 10 per cent silver nitrate and parenteral injections of streptomycin. Such cures usually do not occur with tracheal or bronchial tuberculous lesions, accompanying fibrocaseous pulmonary tuberculosis, or with those remaining in the trachea or bronchi, as a sequel of parenchymatous tuberculosis. We who are in charge of tuberculosis services are aware that it is difficult to totally cure tracheo-bronchial tuberculosis in patients with pulmonary tuberculosis, and in many discharged cases the lesions have reactivated in the same place or its vicinity, even after long endoscopic and parentheral treatments.

The celerity with which these tracheo-bronchial lesions have



CASE 3 CASE 4

Case 3: Beginning Infiltroulcerative Bronchial Tuberculosis, with Positive Bronchial Lavage and no Demonstrable Pulmonary Lesion. Twenty-five year old female has intimately lived with her tuberculous mother for three years. She has no symptom, and reacts to tuberculin. Radiography does not present evidence of pulmonary lesions. Bronchial lavage shows tubercle bacilli. Bronchoscopy reveals infiltroulcerative lesion at the inlet of the bronchus in the right upper lobe.

Case 4: Beginning Ulcerative-Superficial Bronchial Tuberculosis Case—Without Pulmonary Lesions. Bronchial Lavage Revealed Tubercle Bacilli. Twenty-one year old married female has lived with her husband who had contagious tuberculosis. No symptom. X-ray film revealed no evidence of lesion. Bronchial lavage showed tubercle bacilli. Bronchoscopy revealed a superficial ulcerous lesion at the inlet of the bronchus in the upper left lobe.

been cured, with negative bronchial lavage, is another element supporting their precocity and early condition. The absence of serious adenopathies and evident clinical and x-ray findings, as observed in children, permit us to assume that they are not primary infections, but reinfection types of tuberculosis in adults.

The topography of lesions observed in 15 cases is as follows: right bronchi, six; left bronchi, seven; trachea and one bronchus, one; right and left bronchi, one. Predominant anatopathologic conditions were as follows: infiltrative lesions, seven; superficial ulcerative, four; and infiltroulcerative, three. Eleven were females and three were males. Eight were white, one Negro, and five were half-breeds.

From social and epidemiological viewpoints, these cases are of extreme importance, as they may expectorate tubercle bacilli during attacks of acute bronchitis, etc. This finding must create among phthisiologists and hygienists and all physicians a new and modern antituberculosis conscience, leading to the discovery of such cases and treating them promptly to avoid spread of the disease. Moreover if not treated many of these patients become advanced cases of pulmonary tuberculosis.

DISCUSSION

1) Fourteen cases of infiltrative, ulcerative-superficial or infiltro - ulcerative tracheo - bronchial tuberculosis are presented which were detected in the initial stage. Tubercle bacilli were discovered through bronchial lavage. They represent 16 per cent of 95 bronchoscoped cases and 5 per cent of the patients examined.

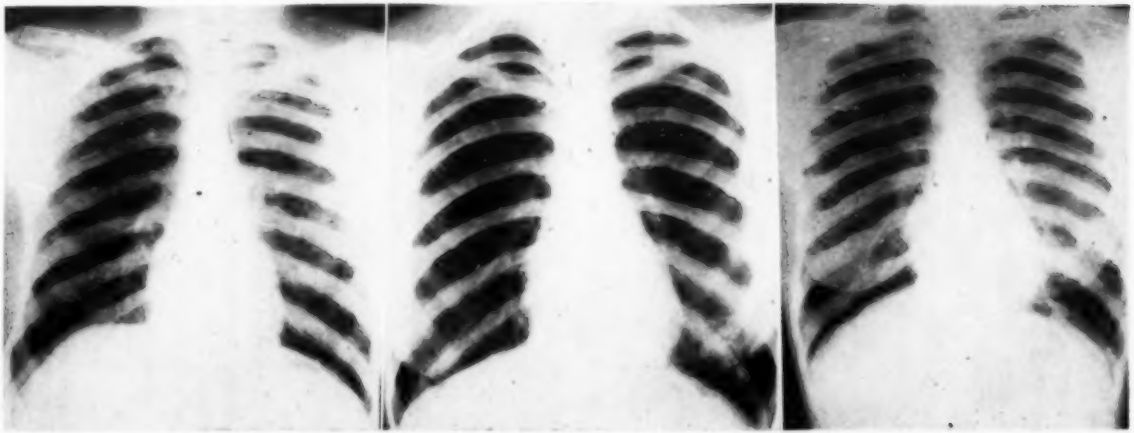
2) One case of this study, which was discovered too late, is similar to the cases previously described by Soulas, Meyer, Capó, Dighiero and others. These cases represent advanced forms of tracheo-bronchial tuberculosis and under no circumstance do they correspond to the begining stage of tuberculosis in the adult, as do the 14 cases we have described.

3) The study of our 14 cases allows us to state that they are not secondary to lesions of the parenchyma. They constitute a completely new syndrome.

4) From clinic, therapeutic, and epidemiologic viewpoints, these asymptomatic forms of begining bronchial tuberculosis give a new projection to phthisiology, and for that reason they should constitute the beginning of a more intense study of the lesions present in persons exposed to contagious cases of tuberculosis in their families.

5) In addition to searching for pleuro-pulmonary tuberculosis through radiography only, we are now also obliged to seek tracheal

CASE 5 CASE 6 CASE 7



Case 5: Beginning Bronchial Tuberculosis Case—Infiltroulcerous Form; no Lesions shown in the Radiography, and Positive Bronchial Lavage. Eighteen year old female has intimately lived with a brother, bacillous tuberculosis case, for a year. She does not present any clinic symptoms, and reacts to tuberculin. Radiography only shows an enlarged pulmonary hilum as sign of cured primoinfection and bronchial lavage with Koch bacilli. Bronchoscopy presents an infiltroulcerous lesion at the inlet of the bronchus in the upper right lobe. — *Case 6:* Beginning Bronchial Tuberculosis Case — Infiltroulcerous form; with no Lesions Shown in the Radiography and Bronchial Lavage with Koch Bacilli. Nineteen year old female has intimately lived with her bacillous tuberculosis sister for two years. She does not present clinic symptoms, and reacts to tuberculin. Radiography does not show pulmonary lesions. Bronchoscopy presents an infiltroulcerous lesion in the main right bronchus.—*Case 7:* Beginning Bronchial Tuberculosis Case—Infiltrative Form, no Lesions Shown in the Radiography, and Positive Bronchial Lavage. Eighteen year old female has lived together with her brother, a bacillous tuberculosis case, for three years. She had no clinic symptoms, and reacted to tuberculin. Radiography presents several calcifications and both pulmonary hilum slightly increased as a sign of cured primoinfection. Bronchoscopy accuses an infiltrative lesion at the inlet of the bronchus in the upper right lobe and in the main left bronchus.

or bronchial lesions by bronchial lavage and bronchoscopy in every person living with tuberculous patients.

6) The presence of tracheal or bronchial tuberculous lesions, without demonstrable pulmonary disease by x-ray film, can be determined only by bronchial lavage and bronchoscopic examination of every contact case.

7) All persons living with tuberculous patients, with positive bronchial lavage, although their x-ray films do not show evidence of lesions, must be bronchoscopically examined for tracheal or bronchial lesions.

8) The systematic application of bronchial lavage as a base of the etiologic diagnosis of the disease, especially in apparently normal exposed persons with no sputa or with negative sputa permits the discovery of numerous hidden cases of pulmonary or bronchial tuberculosis.

SUMMARY

Chest x-ray examination and microscopic tsudy of bronchial washings were made in 500 persons apparently well but who were living in homes of persons who had contagious tuberculosis. Twenty per cent of the 500 cases presented x-ray shadows suggesting tuberculous lesions. In 14 cases of essentially clear x-ray films, tubercle bacilli were recovered from bronchial washings, and lesions in the trachea or bronchi or both were detected by bronchoscopy. The author believes these represent initial reinfection type of lesion in adults, which can be found early only by bronchial lavage and bronchoscopy. He recommends that all intimately exposed persons should have these procedures added to the usual examination for tuberculosis.

RESUMEN

Quinientas personas aparentemente en buena salud pero conviviendo con personas que tenían tuberculosis en etapa contagiosa fueron estudiadas por la inspección a los rayos X y por el estudio microscópico del producto de lavado bronquial.

Veinte por ciento presentaron sombras que sugerían lesiones tuberculosas. En 14 casos de películas esencialmente limpias se encontraron bacilos de la tuberculosis después de lavado bronquial y lesiones de la traquea o de los bronquios o ambas fueron encontradas por broncoscopía.

El autor cree que estas lesiones representan el tipo inicial de reinfección del adulto y que puede descubrirse tempranamente por el lavado bronquial y la broncoscopía.

Recomienda que todas las personas expuestas íntimamente se sometan a este procedimiento de investigación.

RESUME

L'examen radiologique du thorax et l'étude bactériologique des produits de lavages bronchiques ont été pratiqués chez cinq cents personnes. Il s'agissait d'individus apparemment bien portants, mais qui se trouvaient vivre dans les mêmes habitations que des malades atteints de tuberculose contagieuse. Parmi eux, 20% étaient porteurs d'ombres radiologiques qui évoquaient l'existence de lésions tuberculeuses. Dans quatorze cas où les radiographies ne montraient aucune image pathologique, on trouva des bacilles de Koch par lavage bronchique, et la bronchoscopie mit en évidence des lésions, soit dans la trachée, soit dans les bronches, soit à la fois dans les deux organes.

L'auteur pense que ces constatations sont en rapport avec les lésions initiales d'une forme de réinfection de l'adulte dont le diagnostic peut être fait précocément par lavage bronchique et bronchoscopie. Il suggère que toutes les personnes sérieusement exposées à la contagion coient soumises à ces deux examens en dehors des recherches habituelles.

Pneumonia Associated with the Ingestion of Petroleum Products by Children

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The ingestion of petroleum products by children is not infrequent. Some of the more common substances encountered are, benzene, kerosene, gasolene, and insect sprays. Kerosene is the most common poison taken by children.[1] The ensuing irritant and toxic manifestations have been thoroughly described by previous authors.[1-3] However, it is noteworthy that in the clinic, as well as in the literature, most of the emphasis is placed upon the gastrointestinal symptoms, and those associated with generalized intoxication, but it is only recently that our attention is being directed toward the pulmonary signs and symptoms. Whereas it was formerly believed that the pulmonary symptoms were due to the occasional aspiration of a toxic substance, more recent observers contend that this is not always the case, but that the chest findings may be produced by the effect of a toxic agent gaining entrance into the blood stream by way of the gastrointestinal tract.[5-16] Closer observation of clinical material, as well as animal experimentation, indicates that the pulmonary manifestations are an integral part of the intoxication syndrome, and make their appearance in approximately 77 per cent of all cases.[6]

There are numerous references in the literature to poisoning by products of petroleum. Barbour,[7] 1926, reported four cases, one of which was fatal, and Higgins,[8] 1933, recorded another fatal case, and suggested that the serious pulmonary sequelae were due to direct aspiration of the fluid into the lungs. Waring,[9] 1933, working with dogs, and later Lesser,[12] with rabbits, substantiated this conclusion. Nunn and Martin,[10] 1934, and Farbaugh,[11] two years later, showed that the prognosis was directly proportional to the amount of poison entering the lung, and that fatalities usually occurred within 18 hours after the accident. Lesser, Weens and McKey,[12] 1943, produced lung changes in rabbits, only by means of a tracheal catheter leading pariffin directly into the lungs. Cassinelli,[15] also in 1943, described the particular nervous system manifestations associated with broncho-pulmonary involvement. Deichman et al.,[16] 1944, concluded that pulmonary changes were produced by vascular damage, which resulted from

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FIGURE 1a FIGURE 1b FIGURE 2

Figure 1a (Case 1): Chest film made 12 hours after the ingestion of one-half glass of fuel oil. Small, irregular opacities are evident in both lung fields.—*Figure 1b (Case 1):* Chest film made 12 hours after Figure 1a. — *Figure 2 (Case 3):* The pneumonitis is most prominent in the right lower lung field; hilar adenopathy is marked.

the absorption of toxic substances from the gastrointestinal tract. Scott,[14] in the same year, reported a case of pneumonia, pneumothorax and subcutaneous emphysema, complicating pariffin poisoning; Lavenstein,[18] 1945, recorded a similar case.

Steiner,[4] 1947, in his excellent review of 35 cases, divides them into three categories, namely: Group I, acute toxicity and depression of the central nervous system with minimal pulmonary changes, and rapid uneventful recovery; Group II, severe pneumonia, hyperpyrexia and prolonged recovery; Group III, severe pneumonia with evidence of degenerative changes in the myocardium, liver, kidney, and gastrointestinal tract. Lastly, Heacock,[13] 1949, analyzes 156 cases of poisoning in children due to the products of petroleum, and presents an excellent clinical and pathological study.

Case Reports

Case 1: P.H., female, age 18 months, was admitted to the hospital emergency room shortly after drinking about one half glass of fuel oil. The parents stated that the child did cough just after drinking the fluid, and vomiting occurred about 20 minutes later. The stomach was emptied and irrigated with normal saline; bright red blood and oil globules were noted in the emesis. The temperature was 101 degrees F. rectally, and returned to normal in five days. Physical examination revealed inspiratory crepitant rales bilaterally, which lasted four days, and an expiratory grunt and dyspnea, which lasted about 12 hours. There were no symptoms referable to the nervous system. The white cell count was 8,400, with 64 per cent lymphocytes, 29 neutrophils, and 6 monocytes. The urine showed an occasional leucocyte and erythrocyte. Later tests for met-hemoglobin were negative, as were tests for occult blood in the stools.

X-ray film inspection revealed vague mottled densities in both lung fields, with exaggeration and accentuation of root shadows, and bronchovascular markings (Figures 1a and 1b). The right side showed more changes than the left. The child received penicillin by aerosol and by injection, and made an uneventful recovery; however, an occasional cough was noted at the time of discharge, six days later.

Case 2: K.N., female, three years of age, was admitted to the hospital following the onset of hematemesis, after coughing and vomiting for about a day and a half. In this instance there was no clear cut evidence of time, or type of toxic substance ingested, but the child was known to have put coal, which had been coated with oil, in her mouth and ingest it. Subsequent tests for heavy metals, caustics, foreign body, and methemoglobinemia, were entirely negative, hence the impression that the symptoms were referable to the ingestion of fuel oil, was further substantiated.

Temperature on admission was 101.5 degrees F. rectally, respirations 30; pulse 60; systolic blood pressure 95, diastolic 75 mm.Hg. The child had a dry cough, but the only chest findings were a few crepitant rales heard only at the right base posteriorly, during inspiration. The blood count revealed 3,900,000 red cells per cmm., hemoglobin 11.5 grams,

6,900 white cells per cmm., 63 lymphocytes, 33 neutrophils, 2 monocytes, and 2 per cent Turk cells. The urine contained a few hyaline casts, and an occasional red cell. The tuberculin test was negative. There were no central nervous system symptoms, except for an early drowsiness and weakness, which may be attributed to the hematemesis.

X-ray film studies revealed small irregular opacities bilaterally, enlargement of the hilar gland shadows, with a fanning out appearance of the hilar densities. Inasmuch as there was kidney involvement, this case falls into Group III of Steiner's classification. The child received penicillin, and made an uneventful and full recovery in a week.

Case 3: L.S., female, age three and one half years. This child was seen at home after she had swallowed an undetermined amount of kerosene, the previous night. There were no immediate effects, hence the doctor was not called at that time. The next morning the mother noted *coffee-ground* streaks in the emesis, when the child coughed and vomited. Examination at that time revealed a rectal temperature of 104 degrees F., and a respiratory rate of 54. Moist crepitant rales were audible over both bases. The white count was 8,100 cells per cmm, 65 per cent neutrophils, 30 lymphocytes, 5 monocytes. No toxic cells were noted. Sputum examination was negative for pneumococci and acid fast organisms. The urine was normal, but the stool was positive for occult blood, on one occasion. The stomach was not irrigated. The child received aureomycin, and made an uneventful recovery, four days later.

X-ray films revealed a homogeneous density in the right lower lung field, and mottled densities in the corresponding areas of the left lung. The bronchovascular markings were accentuated, and the left hilar region was prominently enlarged. This case also belongs in Steiner's Group III, inasmuch as the blood in the stools and in the emesis indicated extensive gastrointestinal involvement.

Discussion

The foregoing cases illustrate the more common signs and symptoms of poisoning following the ingestion of petroleum products. Usually there is an immediate cough, and choking period, followed by epigastric pain and vomiting. However, in one case (L.S.), this did not occur. As a rule, the infant's immediate condition is not too serious; the more common signs are those of cerebral depression, i.e. drowsiness, collapse and disorientation. Physical findings within the chest are almost always noted upon the initial examination, and x-ray changes have been observed within 30 minutes after the accident.[13]

There is no pathognomonic x-ray picture; the findings will vary with the amount and type of fluid ingested, the duration of illness, and individual constitutional factors. Classically, however, "cotton-wool" opacities of small irregular size, are to be noted bilaterally.[5] Heacock[13] observes that most changes occur at the bases.

None of the cases reported at this time had any complications or sequelae. This is the rule, rather than the exception. The

complications which have been reported in the literature include pneumothorax, empyema, emphysema, pleural effusion, and several deaths.[14-18]

The treatment is generally agreed upon by most authors. Gastric lavage is instituted with utmost caution, inasmuch as aspiration during lavage may contribute to the hazards of complications and even death. If the child has vomited, lavage is best omitted. Therapy with the sulfa drugs, or with antibiotics is instrumental in preventing a secondary bacterial pneumonia from becoming superimposed upon a chemical pneumonia. The sagacity of the use of these drugs is evidenced by the absence of complications and mortality, and the rapid clinical improvement of the youngsters in this series.

There are several schools of thought pertaining to the pathogenesis of pulmonary inflammation as a result of intoxication by hydrocarbons, or products of petroleum. The earliest observers maintained that the pulmonary pathology was the direct result of aspiration of the toxic substance into the lung. This point of view has been adequately expounded by Waring, Lesser, et al., and in all probability is the mechanism exhibited in cases one and two. After sampling the intoxicating fluid, the children no doubt experienced a burning sensation, which in turn caused gasping and choking, and resulted in the aspiration of fluid into the lung. Because of the low volatility of these hydrocarbons, they were not expelled by the expiratory air currents, but remained in the alveoli to produce the pathology characteristic of aspiration pneumonia.

The third case exemplifies the thought of another school, which maintains that the toxic substances are absorbed through the gastrointestinal tract into the blood stream and are carried to the lung where they are eliminated. In this role as an excretory organ, the lungs probably suffered their pathological changes. In the aforementioned case, it will be noted that the child did not gag or choke, hence there is little possibility that any of the fluid was aspirated, so we must assume that most of the kerosene reached the lung by way of the blood stream. Finally, a third pathogenesis is offered by Casselli,[15] who maintains that inhalation of the volatile vapors of certain products of petroleum, may result in pneumonic pathology.

SUMMARY

1) Cases of pneumonia associated with poisoning by products of petroleum are presented.

2) The several schools of thought pertaining to the pathogenesis

of pulmonary symptoms are discussed, and exemplified by the foregoing cases.

3) The value of chemotherapy and antibiotic therapy is stressed, and is responsible for the relatively low morbidity and the absence of mortality.

4) Attention is directed toward the pulmonary manifestations of cases of poisoning, and roentgenological changes are described.

RESUMEN

1) Se presentan casos de neumonías asociados a envenenamiento con productos del petróleo.

2) A partir de los casos presentados, se discuten las diversas escuelas que explican la patogenia de los síntomas pulmonares.

3) Se hace énfasis sobre el valor de la quimioterapia y de los antibióticos y al uso de ellas se atribuye la escasa morbilidad y la ausencia de mortalidad.

4) Se llama la atención sobre las manifestaciones pulmonares en casos de intoxicación y se describen los cambios radiológicos.

RESUME

1) L'auteur rapporte des cas de pneumonie survenant chez des individus empoisonnés par des produits pétrolifères.

2) Il discute les différentes théories qui peuvent être émises au sujet de la pathogénie des symptômes pulmonaires en se basant sur les observations précédentes.

3) Il met l'accent sur la valeur de la chimiothérapie et des antibiotiques qu'il tient pour responsables de la morbidité relativement basse et de l'absence de mortalité.

4) Il attire l'attention sur les manifestations pulmonaire accompagnant les empoisonnements et il en décrit les manifestations radiologiques.

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Epiphrenic Diverticulum of the Esophagus

A Review of Its Surgical Treatment and Report of a Case*

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Articles embracing the incidence, etiology, differential diagnosis, symptoms and complications of epiphrenic diverticulum of the esophagus have appeared not too infrequently in the past.[5,9,11,17,18,21,27,28,30,31] However, except for the notable contributions of Janes,[13] Adams,[1] and Harrington,[10] the surgical aspects of this disease have received scant attention. No article has appeared which considers earlier experiences and thoughts on the surgery of such lesions since the contributions of Lotheissen[16-18,31] more than two decades ago. For these reasons, it is felt worthwhile to review in some detail the surgery of such diverticula from the historical standpoint as well as present trends in treatment.

The first proposal for the surgical extirpation of such lesions appeared in 1901, when Enderlen[6] suggested that they be removed through a posterior mediastinotomy, an operation conceived by Nassiloff in 1888 and first performed a decade later by Rehn.[22] On the basis of the few clinical and autopsy cases of such diverticula then known, Enderlen concluded that surgical intervention was rarely indicated and could then be only infrequently attempted, since he considered the following theoretical criteria prerequisites to surgery: 1) The diverticulum must not lie below the level of the ninth thoracic vertebra. 2) It must be free from adhesions with surrounding structures. 3) The pedicle must not be too large. 4) Carcinoma must not be a complication. 5) Excessive malnutrition must not be present. An alternative procedure suggested by Lotheissen[16] in 1908, proposed anastomosing the fundus of the diverticulum to the cardia of the stomach (marsipogastrostomia) through an abdominal approach and incising the diaphragm to gain access to the diverticulum. He also considered the use of the Murphy button in lieu of suture, recognizing the difficulty of esophageal suture. Since diverticula at a higher level would not be accessible by such an approach, he briefly suggested the possibility of transpleural resection.

Although Dessecker[5] credits Enderlen as the first to operate for

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an epiphrenic diverticulum, the case of Roux,[23] operated on in 1906, probably deserves priority, although it was not strictly epiphrenic in nature. This lesion was approached by laparotomy and found on the subphrenic portion of the esophagus. Being small, it was incised, obliterated by stretching, and the ensuing defect plicated with uneventful recovery and cure. Enderlen's[7] case reported in 1910 was in a severely emaciated man of 62 years who had preliminary gastrostomy three weeks prior to excision of the diverticulum. Exposure was obtained by a paravertebral extrapleural resection of the third through the seventh ribs on the left side as previously proposed by him. The sac was excised and the defect sutured. Death occurred 26 hours postoperatively of heart failure and autopsy revealed the suture line to be intact. As subsequently commented upon by Lotheissen,[31] this again was probably not an epiphrenic diverticulum because of its high location. That a cervical approach would have been possible as assumed by Lotheissen is doubtful, since he erroneously states that the first through the fourth ribs were resected. It probably represented a rare, large, and symptomatic epibronchial diverticulum of the traction-pulsion variety.

In 1916 Stierlin[29] reported the transthoracic excision of an epiphrenic diverticulum which ended fatally because of fistulization of the suture line and mediastinitis. Clairmont[4] in 1924 reported the case of a 43-year old woman suspected of having carcinoma of the distal esophagus. Subsequent to jejunostomy the esophagus was freed for a distance of 10 centimeters above the cardia and the esophagus pulled down into the abdomen. An epiphrenic diverticulum was discovered, excised, the defect closed with one layer of sutures, and the esophagus allowed to return into the mediastinum. Healing occurred without incident. Sauerbruch[24] had several cases with severe symptoms unrelieved by a conservative regimen that warranted operation. In two instances an anastomosis was made between the cardia of the stomach and the diverticulum as initially proposed by Lotheissen. The first case terminated fatally from mediastinitis, while the second case, done by Henschen in Sauerbruch's Clinic, was successful. A third case was complicated by dense adhesions between the cardia of the stomach, diaphragm, and diverticulum. For this reason anastomosis was not felt necessary, and a gastrostomy was performed and the diverticulum entered by cutting down upon a previously placed esophageal sound. This patient recovered and was apparently cured.

Although no direct reference is to be found, Lotheissen[31] in 1926 reported that Willy Meyer successfully excised such a divetriculum transthoracically. Sauerbruch[25] in 1927 reported another case suc-

cessfully excised by transpleural excision using his differential pressure chamber. In this case the neck of the sac was transected between clamps and closure accomplished by three layers of invaginating sutures. A pedicle from the previously paralyzed diaphragm was employed to reinforce the suture line. Convalescence was uneventful and symptoms disappeared. An additional excision by the posterior extrapleural route was reported by Quartero[20] in 1931. The right 10th and 11th ribs were resected, the pouch excised, and closure obtained with a double row of sutures. On the eighth postoperative day a fistula appeared, but the patient went on to recovery with subsequent spontaneous closure of the fistula.

In 1933 Barrett[2] reported a case successfully excised transthoracically by Romanis through an intercostal incision. The neck of the sac was clamped and transected with a diathermy knife and closure effected with a double row of catgut sutures, a pleural flap being employed to cover the suture line. Postoperative convalescence was uneventful. This case was correctly reported as an intrathoracic esophageal diverticulum, and not one of the epiphrenic variety, a category given to it by subsequent authors, since it is to be noted that the neck of the sac was located at the level of the azygos vein.

Diverticulopexy, first advocated by Schmid[26] in 1912 and first employed by Hill[12] in 1917 for pharyngoesophageal diverticula, has also been applied to those of the epiphrenic variety, Lahey[15] apparently being the first to utilize this method for the latter type. Adams[1] discusses three cases of diverticulopexy for epiphrenic diverticula done in the prechemotherapeutic era, in old, poor risk patients with excellent results. In none was co-existing cardiospasm present. In the same article Adams reported five other cases treated by primary transpleural excision. The technique employed was to free the pouch, dissect the neck down to the mucosa and to place a straight clamp across the neck 0.5 centimeters distal to the wall of the esophagus. The mucosa was invaginated with a running Cushing stitch and reinforced with a muscle layer of interrupted silk, the mediastinal pleura being closed over it. In this series there were no deaths nor complications. Janes[13] reported four successful cases of transthoracic diverticulectomy in which the neck was clamped with three straight clamps with transection between the two distal ones, the middle clamp removed and the fringe oversewn with a running catgut stitch, the proximal clamp removed, and the first row invaginated by interrupted Lembert sutures. Finally, the incised mediastinal pleura was closed behind the esophagus, feeling that mediastinitis is thus less likely and that the pleural cavity is better able to

withstand infection should it occur. Harrington,[10] on the other hand, feels that the median fold of the mediastinal pleura should be sewn over the esophageal suture line, but that the posterior fold be left open for drainage. He stresses the importance of separating only sufficient mediastinal pleura necessary to expose the sac, minimal separation of the esophagus from its bed, and the necessity of complete separation of the herniated mucosa from muscle wall. Excision is carried out 1.5 centimeters from the opening into the esophagus over a right angle clamp, the mucosa inverted with a Connell suture, and the muscle closed with a double layer of interrupted silk sutures. Of eight cases reported by him, transpleural excision was accomplished in seven, and in the other, invagination of a small sac with plication of the dilated esophageal wall was done. One patient developed an empyema which responded to thoracotomy drainage. One fatality ensued subsequent to pneumonia and a localized mediastinal abscess. It is of interest to note that six of Harrington's cases had an associated esophageal hiatus hernia. In only one was repair required. Vinson[30] noted hiatus hernia associated with intrathoracic esophageal diverticulum only once in 42 cases, and Granet[9] found this complication only once in 31 cases collected from the literature. The high incidence of such herniae in Harrington's series would tend to question the previous concept that the association of these two lesions is uncommon. The only other report of a successfully excised epiphrenic diverticulum found in a review of the literature is that of Kay.[14] Of two cases associated with short esophagus, one failed to respond to conservative therapy and was successfully excised transthoracically.

In attempting to assess the divergent attitudes toward this lesion, little unanimity of opinion can be found concerning many of the problems presented. The etiology must be considered as unknown, for although somewhat less than half of the reported cases have an associated cardiospasm, there is as much evidence to consider the diverticulum secondary to the cardiospasm as in the reverse order. In this respect, the case of Poppe and Berg[19] is of interest. Their patient had severe cardiospasm associated with a large diverticulum. Repeated dilatation and other conservative measures failed to alleviate the symptoms. On the debatable assumption that the symptoms in such instances are on the basis of the cardiospasm, which in turn is secondary to the diverticulum, a diverticulopexy was performed without benefit, and a subsequent anastomosis of the sac to the cardia of the stomach resulted in symptomatic relief. In partial support of their view, they have quoted Dessecker[5] as reporting two cases of epiphrenic diverticulum, both with cardiospasm. Perusal of this article reveals that

Dessecker reported but one case not associated with spasm. Concerning this problem, Raven[21] felt that "the most reasonable supposition is the presence of distal esophageal obstruction with increased pressure, causing herniation of the mucosa in an area where muscle coats have been weakened by local esophagitis." Smith[28] concluded that deep diverticula are of no importance in the etiology of cardiospasm. The failure of diverticulopexy in the case of Poppe and Berg would appear to argue against such a causal relationship, for one would expect this procedure to have been successful if such a relationship held. Finally, in Janes[13] series, one patient had esophageal spasm, and Harrington[10] noted cardiospasm in three of his cases, yet both authors reported favorable results following resection despite the cardiospasm.

Those cases complicated by hiatus hernia or short esophagus also fail to elucidate the development of such diverticula. One is then reduced to a consideration of those instances where the diverticulum exist independently of such lesions, and here no patent explanation of their origin exists. Several theories have been advanced, such as congenital weakness of the muscular layers, or herniation through weak areas surrounding the nutrient vessels. For a more detailed review of such theories the reader is referred to the articles of Lotheissen, Dessecker, and Janes.

In most instances the diagnosis is not difficult. Though mild dyspepsia may be the sole symptom, dysphagia, epigastric or substernal pain, regurgitation, eructation and even vomiting after meals in conjunction with anorexia and weight loss are characteristic. Esophagoscopy and barium studies will substantiate the nature of the lesion. Some confusion may be encountered in interpreting roentgen studies in which a cardiospasm is accompanied by a large sigmoid dilatation of the distal esophagus, and in esophageal carcinoma, which occasionally causes the formation of a pseudo-diverticulum. In this respect, it is of interest to note that four cases of true epiphrenic diverticulum, complicated by carcinoma, have been reported.[31]

The attitudes regarding the significance of epiphrenic diverticula can best be illustrated by the extremes; Heacock[11] maintaining that they are of little clinical importance, their chief interest lying with the anatomists and the roentgenologists, while Dessecker[5] felt that all such diverticula eventually led to a lethal outcome. Asymptomatic lesions are probably best left untreated; however, those in which symptoms exist, therapy should be instituted. If an associated cardiospasm is present, symptomatic relief can be expected in some instances following dilatation. If relief is not obtained, surgical intervention should be undertaken. The existence of a paraesophageal hiatus hernia or a short esoph-

agus may make it difficult to actually evaluate which lesion is producing the symptoms; nevertheless, it would appear from the literature that surgical excision of the diverticulum will result in cure, although reduction of a hernia may also be necessary. Of all the various surgical approaches and methods which have been employed, only two appear to have any great merit. In extremely poor risk patients, who have no associated cardiospasm, transthoracic diverticulopexy would appear to be a relatively safe and satisfactory procedure. In other instances, a direct transthoracic excision of the lesion seems to be the treatment of choice. The earlier, indirect methods are of historical interest only and should be regarded as a phase in the evolution of esophageal surgery. The present-day esophagogastrostomy, as carried out for carcinoma of the distal esophagus, has not been utilized for the surgical treatment of epiphrenic diverticulum. However, in instances associated with intractable cardiospasm, it may well represent the proper procedure. Although Biondi[3] was the first to propose this type of esophageal resection specifically for carcinoma in 1895, Gosset[8] independently described the same procedure in a classical paper in 1903 and felt that it might also be used for benign lesions such as diverticulum and cardiospasm as well as for carcinoma. Because of the infrequency of the lesion under discussion and the relatively small number which have been treated surgically, the following case is being reported.

Case Report

(New Haven Hospital C9963) G.Z. A 53-year old Italian housewife was admitted on April 16, 1948 because of epigastric pains. Two years previously she experienced her first attack, characterized by the sudden onset of severe sharp pain just below the xiphoid and radiating along the left costal margin. There was no dysphagia, nausea, or vomiting, but pain was intensified by swallowing, particularly solids. After one week the patient noted marked improvement, although she still had occasional mild epigastric pain of short duration during or after meals. From this time until admission she limited her diet to soft pureed foods and liquids, since solids caused her more distress. Three weeks prior to admission she again had an abrupt onset of persistent severe epigastric pain following a meal. This was initially sharp, but became gnawing in character radiating along the left costal margin and into the mid-back. Solids and to a lesser extent fluids intensified these symptoms. She was placed on antacids, but failed to improve. Some relief was noted when lying on her right side. There was no vomiting, but there was gaseous eructation and regurgitation of sour fluids. During this three week episode the patient lost 12 pounds. There was no history of icterus, acholic, tarry, or bloody stools, hematemesis, or change in bowel habits. Family and past history were not contributory and system review revealed only irregular menses and occasional menorrhagia.

Upon physical examination the vital signs were: temperature 98 degrees F., blood pressure 144/84, respirations 22, pulse 80. The positive

findings were limited to abdominal and pelvic examination where there was moderate tenderness and voluntary splinting upon deep pressure in the epigastrium, cervical erosion, lacerations, and polyps. Laboratory data revealed a blood count of 4.43 million red blood cells with 13.5 grams hemoglobin, 8,600 white blood cells with a normal differential. Mazzini blood test was negative. Urinalysis, N.P.N., proteins, and chlorides, and an EKG were within normal limits. Roentgenologic examination revealed a smooth, rounded, soft tissue mass, measuring about six centimeters in diameter just to the right and adjacent to the lower third of the esophagus and displacing it slightly to the left. Following the ingestion of barium, direct continuity between the lumen of the esophagus and the previously described mass could be noted with a small amount of barium entering the mass, but incompletely filling it (Figure 1). The wall of the esophagus itself did not appear to be involved; it was dilatable, and changed shape readily. There was no evidence of obstruction to the flow of barium down the esophagus, although there was a slight holdup of the barium at the site of the diverticulum. There was no abnormality of the esophagus distal to the diverticulum, and the stomach, duodenum, and small bowel were normal. A small amount of barium was noted in the diverticulum at the end of five hours. Esophagoscopy demonstrated

Figure 1: Barium swallow revealing poor filling of the diverticulum because of foreign body. The outline of the pouch can be seen however.

a normal esophagus up to the level of 40 centimeters from the upper gum margin, at which point the mouth of the diverticulum was noted at 5 o'clock with the esophageal lumen continuing at 11 o'clock. The sac was filled with foreign body material, and an attempt was made to irrigate this out unsuccessfully. As much was removed by biopsy forceps as possible. Pathological examination of this material revealed it to be composed of vegetable fibers and amorphous debris. Because the previous study of the esophagus had revealed poor filling of the diverticulum, the question of carcinoma within it was raised and a repeat study was done, which again showed poor filling and was essentially unchanged from the previous examination. On April 23, 1948 the patient had excision of a cervical polyp, with biopsy of the cervix, and a dilatation and curettage under intravenous pentothal. Pathological report of the tissue removed showed cervical polyp, chronic cervicitis, and local endometrial hyperplasia.

Postoperatively the patient recovered rapidly from this procedure, and three days later under general endotracheal anesthesia, the left chest was entered through the bed of the ninth rib. After division of the pulmonary ligament and retraction of the left lower lobe, the distal esophagus was freed up just above the cardia and a Penrose sheath placed about it for traction, following which it was possible to identify a large-mouthed diverticulum passing from the posterior aspect of the esophagus into the mediastinum between the descending aorta and the pericardium. The proximal esophagus just above the pouch was freed up bluntly and a second Penrose sheath placed about it for traction. By elevating both tractors it was possible to progressively dissect the very adherent sac from the surrounding structures. The sac itself extended through the thickened muscular layer of the esophagus out into the mediastinum as a well defined thick-walled pouch. It was necessary to place considerable traction on the descending aorta in order to get a good visual field. Finally the entire pouch was delivered without opening it and gauze placed beneath it to protect the mediastinum. The neck of the sac was then opened because of the feeling that carcinoma might be present, and a large amount of decaying gauze was extracted from the sac. When it was completely empty, it was seen to be lined with a mucosa continuous with the esophageal mucosa itself. There was no evidence of local tumor. The sac was excised and then the esophageal wall was repaired by placing inverting sutures of interrupted No. A silk to the mucosa followed by interrupted No. A silk sutures to the thickened muscular layer. This was further reinforced with a plaque of gelfoam. The mediastinal defect where the sac originally lay was thoroughly irrigated with saline, a few crystals of sulfanilimide powder dusted into the wound, and the esophagus replaced in its normal position after rotating it in its usual axis. No attempt was made to close the mediastinal pleura in order to permit drainage into the left pleural cavity. The left pleural cavity was irrigated with saline solution, 100,000 units of penicillin introduced, and the chest closed in layers with an interrupted silk technique.

The patient had received whole blood and electrolytes during the procedure and was maintained on intravenous therapy postoperatively for a period of five days being kept on constant gastric suction for this same period. In addition, she received parenteral vitamins, sodium sulfadiazine and penicillin. At the end of five days the gastric tube was removed

and the patient started on 30 cc. of water every hour which was well tolerated. Fluids by mouth were rapidly advanced, and the patient was on a Sippy III diet at the time of her discharge 12 days postoperatively.

Pathology: The foreign body removed from the diverticulum consisted of two pieces of dark, yellow-brown masses each 1 x 1.5 x 4 centimeters in size and having a granular, laminated structure. On histologic examination, mononuclear, polymorphonuclear and stratified squamous cells were noted lying in a framework of acidophilic vegetable cells and fibers. The diverticulum itself was a roughly hemispherical sac 3 centimeters

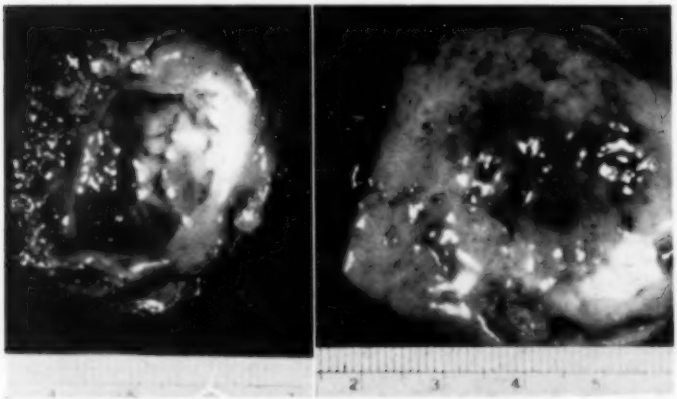

Figure 2: Photograph of gross specimen revealing wide mouth and thickened wall on the left. Specimen evaginated on the right to demonstrate ulceration.

Figure 3: Low power view showing normal mucosa on the right and ulcer on the left. Only a few muscularis mucosa fibers are present, the remaining portion of the wall being composed of fibrous tissue.

in depth with an orifice 3.5 centimeters in diameter having an irregular wall measuring 0.9 centimeters at one margin and about 0.3 centimeters at the other. The sac was lined with a dull-white membrane defective in two places. One defect was at the very depth of the sac measuring 0.4 centimeters in diameter and covered with dark, red, sanguinous material. The other was linear, two centimeters long but widened to a crater 0.6 centimeters in diameter at one end and covered with a fibrinous, dull, yellow material (Figure 2) Microscopically the sac was lined with stratified squamous epithelium save in the ulcerated areas, one of which was shallow with a connective tissue base infiltrated with mononuclear and polymorphonuclear cells and containing a superficial layer of necrotic tissue. The other ulcer showed chronicity being deeper and composed of a thick base of granulation tissue. The wall of the diverticulum consisted of dense connective tissue containing lymphocytes and plasma cells. The only muscle fibers noted were interlacing bundles of smooth muscle immediately under the epithelium and representing muscularis mucosa (Figure 3).

Comment

In this case, the occurrence of an unexplained foreign body and ulcer formation quite likely explains the recent exacerbation in the patient's symptoms and exemplifies two complications of such esophageal diverticula which justify surgical treatment. Ordinarily, it is neither necessary nor expedient to open the sac at operation; however, the possibility of a carcinoma in this instance warranted such a procedure. The pathology in this case was in no way unusual. The absence of the muscular layers is characteristic of such diverticula in contradistinction to the traction type where all layers of the esophageal wall are represented.

SUMMARY

1) A review of the surgical management of epiphrenic diverticulum of the esophagus has been presented. An evaluation of the various surgical procedures would indicate that transthoracic excision is relatively safe, accompanied with good results and probably the method of choice in most instances.

2) A case of epiphrenic esophageal diverticulum complicated by foreign body and ulcer formation is reported. Surgical excision of the lesion was successfully accomplished.

RESUMEN

1) Se presenta una revisión del tratamiento quirúrgico del divertículo epifrénico del esófago. Una evaluación de los diversos procedimientos quirúrgicos indicaría que la excisión transtorácica es relativamente segura, se acompaña de buenos resultados y es probablemente el método de elección en la mayoría de los casos.

2) Se relata un caso de divertículo epifrénico esofágico complicado con cuerpo extraño y ulceración. La extirpación quirúrgica de la lesión fué llevada a cabo con éxito.

RESUME

1) Les auteurs présentent une revue générale du comportement chirurgical en présence d'un diverticule diaphragmatique de l'oesophage. L'évaluation des différentes techniques chirurgicales tend à montrer que l'intervention trans-thoracique est relativement sûre; les résultats en sont bons, et il est probable que dans la plupart des cas, c'est une méthode de choix.

2) Ils rapportent un cas de diverticule diaphragmatique de l'oesophage compliqué par un corps étranger, avec constitution d'ulcération. L'exérèse de la lésion put être réalisée avec succès.

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Pulmonary Histoplasmosis: Report of a Case Long Considered Tuberculous Improved by Acti-Dione*

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Histoplasmosis in endemic areas such as the Mississippi Valley is now considered to be the cause of many instances of pulmonary calcification formerly thought to be tuberculous.[1-5] We wish to report a case who had a pulmonary infection in 1918-19 which from 1925 to 1949 was considered to be tuberculous although tubercle bacilli were never demonstrated. Skin test and complement fixation were positive for histoplasmosis. Histoplasma capsulatum was cultured from sputum and lung tissue and was demonstrated in lung tissue removed by lobectomy. He improved clinically and the sputum no longer showed histoplasma after intensive treatment with Acti-dione.

Case Report

This 51 year old white male was admitted October 29, 1949, for treatment of pulmonary tuberculosis. Following an attack of influenza in France in 1918, he had a severe productive cough and remained in quarters for three months. He was discharged from the army March 20, 1919, apparently well. His first hospitalization here began July 24, 1925. He complained of chest pain, weakness and cough intermittently since three weeks after discharge from the army. Stereoscopic roentgenograms of the chest in July showed a slight deviation of the trachea to the right, increased hilar densities, and slight haziness in the right apex, first and second interspaces. Stereoscopic views in December showed decrease of the haziness in the right apex, persistence of the hilar shadows and the presence of a filmy infiltration of the entire left upper lobe. Physical findings were not remarkable except for constant medium rales over the right apex. He weighed 140 lbs. and stood 5 ft. 10 in. Urinalyses, serology and blood counts were normal. Fourteen sputum examinations were negative for acid fast bacilli. There is no record of sputum culture or animal innoculation. He was discharged against medical advice January 21, 1926, because his wife and son allegedly were ill with tuberculosis. The discharge diagnoses were: arrested pulmonary tuberculosis and chronic fibrous pleurisy.

On July 17, 1926, he was readmitted with the previous complaints of

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pain in the chest. X-ray examination still showed increased hilar shadows. The pleura appeared to be thickened in both apices. Physical examination was negative. He weighed 143½ lbs. Leucocytes were 10,960 c. mm. with 60 per cent polymorphonuclears, 32 per cent lymphocytes and 8 per cent large mononuclears. Ten sputum samples were negative for acid fast bacilli. He produced 3 cc. sputum per 24 hours. He was discharged July 31, 1926, with the previous diagnoses and not considered in need of treatment.

From 1926 to 1949 he had been able to work as a blacksmith, although the cough persisted and he was frequently seen by his family doctor. A chest x-ray film taken in a Veterans Administration Regional Office June 21, 1949, was fairly normal (Figure 1). In August he noted temperature elevations from 99 to 100 degrees F. daily. In September he experienced sharp pains in both sides of the chest, fever rose to 104 degrees F. and "hovered around 102 degrees F. for two weeks," and he was treated with a sulfa preparation and penicillin for "pneumonia." A follow-up chest x-ray film revealed pathology in the right lung and his physician advised hospitalization. He was admitted to the tuberculosis service October 29, 1949.

Physical examination showed a well developed, poorly nourished, 51 year old white male who appeared chronically ill. Temperature: 99.5 degrees F. Pulse: 78 per minute. Respiration: 18 per minute. Weight: 129 lbs. Blood pressure: 102/62 mm. Hg. Most of the teeth were missing, those remaining were carious and pyorrhea was present. There was mild bilateral deafness. Chest expansion was poor. The liver and spleen were not palpable. There were external hemorrhoids. Otherwise the physical examination was within normal limits.

Laboratory findings: On admission: erythrocytes 4,850,000, hemoglobin 13.5 gms., leucocytes 11,200 of which 69 per cent were neutrophils, 20 per cent lymphocytes, 7 per cent monocytes, and 4 per cent eosinophils. Cutler sedimentation rate was 22 mm./hr. Specific gravity of the urine was 1.010. Albumen, sugar and casts were absent. Kahn was negative. Twenty cc. of mucopurulent sputum was produced per 24 hrs. Daily sputum specimens were negative for acid fast bacilli and many cultures were likewise negative for tubercle bacilli. On December 12, 1949, Histoplasma capsulatum was identified in culture from a sputum specimen of November 25.* Four other samples were subsequently positive. Several cultures for acid-fast bacilli from sputum, gastric and bronchial washings were discarded as negative after 90 days incubation. Skin test with histoplasmin (1:100 dilution) produced an area of induration 20 mm. in diameter without erythema in 48 hrs. Complement fixation for histoplasmosis was reported positive 1/32 on two samples a month apart.† The leucocytes reached a maximum of 26,100 c. mm. The highest Cutler sedimentation rate was 30 mm./hr. X-ray film inspection of the chest on admission showed evidence of cavitary disease in the right upper lobe with infiltration of a mixed character extending downward to the level of the fourth anterior interspace. The left lung was essentially clear. Chest x-ray film taken January 10, 1950, showed a fluid level in the cavity and some spread to the left pericardiac area (Figure 2).

*Identification of the culture was confirmed by Arden Howell, Jr., Ph.D., Chief, United States Public Health Service, Medical Mycology Laboratory, Duke University.

†By United States Public Health Service, Chamblee, Georgia.

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1: Relatively normal roentgenogram taken June 21, 1949.—*Figure 2:* Roentgenogram taken January 10, 1950, showing a fluid filled cavity and mixed infiltration in the right upper lobe and early spread to the left pericardiac area.—*Figure 3:* Roentgenogram typical of recovery phase. Taken January 9, 1951.

After Histoplasma capsulatum was recovered the patient was transferred to the medical service. Sulfadiazine gm. 1 q. 4 hr. was given for one week without effect on the daily temperature elevation to 100-100.8 degrees F. No endobronchial disease was demonstrated by bronchoscopy.

Before the diagnosis was established, exploratory thoracotomy had been considered. Finally it was decided that since most of the detectable disease was in the right upper lobe, lobectomy would remove this and afford a better chance for the bodily defense mechanisms to overcome what remained. There was no evidence of generalized histoplasmosis. Accordingly therefore, the right upper lobe was removed by Dr. Louis F. Knoepp on January 27, 1950. The apical and posterior segments of the lobe were so densely adherent that they had to be literally excised from the parietal structures. Small nodules could be felt in the middle lobe and superior segment of the lower lobe but these were not disturbed because of the x-ray evidence of involvement of the left lung. Histoplasma capsulatum was cultured from the removed lung as well as demonstrated in sections of it as shown in Figure 4. The post-operative course was uneventful. On the 19th post-operative day he went home for a 14 day visit.

On February 5 the temperature suddenly rose to 103.2 degrees F. and he was returned to us for treatment. He weighed 132 lbs. Two days later the temperature spiked to 104 degrees F. Chest x-ray film showed an increase in pathology in the left upper lobe. Two hundred seventy five cc. of dark gray-green sputum was produced in 24 hours. Intramuscular penicillin 50,000 units every three hours was begun March 9 with a

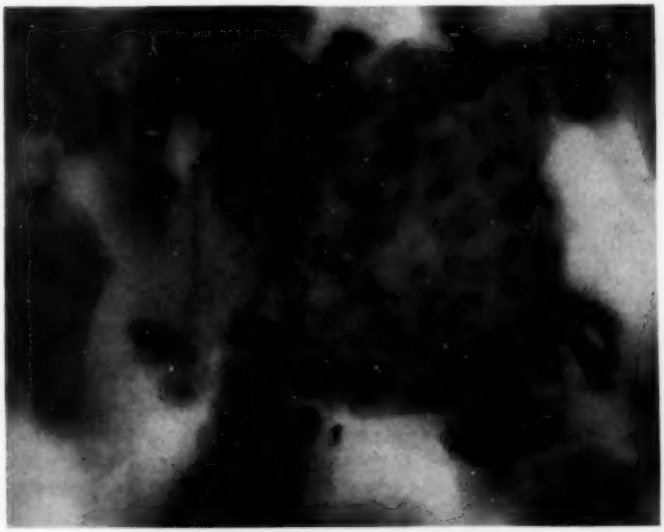

FIGURE 4: Histoplasma capsulatum in section of lung. (Hematoxylin and eosin 1200x).

prompt decline in temperature to 99-100 degrees F. and decrease in the volume of sputum to 120 cc. although its character remained unchanged. Therapy with Acti-dione* 60 mg. intravenously daily was begun March 13. Sputum obtained that day grew H. capsulatum. Within 24 hours the temperature was normal and the volume of sputum reduced by one half. On March 16 penicillin was discontinued. He remained afebrile thereafter and the sputum became thinner and averaged only 15-20 cc. per 24 hours. Only one specimen (March 24) during this period was positive. This was the last time histoplasma could be recovered from the sputum. The daily administration of Acti-dione was continued through May 18 at which time he went home without medication. He returned May 23 with chest pain, temperature of 103.4 degrees F. and respirations of 32 per minute. The day before he had had a chill. Sputum was increased. Acti-dione was resumed with prompt improvement. Bone marrow culture started June 1 was negative. On July 4 the dose of Acti-dione was reduced to 40 mg. daily. On August 9 he weighed 141 lbs., brought up 3 cc. clear sputum, and Acti-dione was discontinued. All was well until August 20 when he experienced chills with fever to 101 degrees F., and the next day sputum increased to 45 cc. Acti-dione 40 mg. daily was resumed. After five days he was afebrile and sputum was reduced to 5 cc. per 24 hours. On September 23 the dose was reduced to 20 mg. and on September 30 it was discontinued. Daily sputum cultures from October 2 through 6 were negative. He remained afebrile, sputum was scanty and weight was 145 lbs. so he was sent home on leave. Random specimens collected October 11, 12, 18, 19, 24 and 25 were negative. October 18 he returned with a history of chills, temperature was 100.2 degrees F., sputum was 15 cc. daily, and he had lost 7 lbs. He was then started on Acti-dione 25 mg. orally daily.* On October 30 the dose was increased to 25 mg. b.i.d.

This medication was not discontinued until January 5, 1951. There was no exacerbation and he was discharged from the hospital January 25, 1951, feeling "the best I have in years" and weighing 144 lbs. Leucocytes were 5,950 c. mm. with 44 per cent neutrophils, 44 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils. Erythrocytes were 4,820,000 c. mm. Hemoglobin was 14.8 gm. Cutler sedimentation rate was 8 mm. per hour. There had been no essential change in the chest x-ray film since September 1950. An x-ray film representative of this period is shown in figure 3. Sputums obtained January 8, 9 and 24 were sterile. The last one was held until March 3, 1951, without growth.

Six weeks after discharge he advised us by letter that he was still asymptomatic and afebrile.

Discussion

Although this patient's wife and son were thought to have pulmonary tuberculosis in 1925, neither that nor histoplasmosis was proved. The son served in the army in World War II and is clinically healthy. The wife has been under a physician's care

*Furnished by Dr. H. F. Hailman, the Upjohn Company, Kalamazoo, Michigan.

*Supplied by Dr. J. W. Frost, Eli Lilly and Company, Indianapolis 6, Indiana.

for frequent respiratory infections without the demonstration of an etiologic agent.

Histoplasmosis and tuberculosis have been reported in the same individuals.[6,7]

Furcolow[7] has emphasized that histoplasma may be found in a wide variety of clinical conditions in some of which it seemed to be an incidental finding of academic rather than practical importance. We believe the diagnosis of histoplasmosis is clearly established in our case and that the diagnosis of pulmonary tuberculosis was never proved. If we are to assume that pulmonary histoplasmosis existed from 1918-19, why was it relatively mild for so long? Why did it become more active with higher temperature and more sputum production in 1949-50? The chest x-ray film was relatively normal in June 1949 so that "pneumonia" in September may have been the initial infection with Histoplasma. However, the possibility of a fungous infection was not considered until November 1949.

The portal of entry of the fungus in man is not clearly established. The organisms have been demonstrated in the lungs of experimental animals innoculated intranasally and in the livers and spleens of animals infected orally.[8] It would seem, then, that our patient was infected through the respiratory tract.

The histoplasmin skin test in either 1:1000 or 1:100 dilution is reportedly of value if induration and not erythema is considered a positive test.[4] Many persons who are positive to histoplasmin and negative to tuberculin show other evidence of histoplasmosis. The skin test, however, may be negative in histoplasmosis. It is only suggestive, not diagnostic.

The complement fixation test has been positive in many proved cases but cross reactions with other fungi have been demonstrated. So it, too, must not be relied upon when unsupported by other findings.

The best diagnostic feature, therefore, is the repeated isolation of the fungus from cultures of blood,[9] sputum, gastric washings, bone marrow, or tissue.

Either recovery or death may occur. Many of the recovered cases were exclusively pulmonary in location while the fatal cases often showed infection of lymph nodes, liver, lungs, spleen, adrenal glands, intestines, bone marrow, kidneys and oropharynx[10,11] in order of decreasing frequency.

No effective method of treatment has been established. Lobectomy has been performed by others.[10,11] We were unable to inhibit this patient's strain of Histoplasma capsulatum in vitro with various concentrations of Acti-dione. No animal experiments were conducted.

The patient's sputum was reduced in quantity, his fever disappeared, weight and sense of well being improved, and H. capsulatum could no longer be cultured from the sputum after a prolonged course of Acti-dione. Several febrile exacerbations were promptly controlled by re-administration of the drug. We believe the improvement was more than coincidental and therefore Acti-dione merits further study in cases of histoplasmosis.

SUMMARY

A case* is presented who had a chronic cough following "influenza" in 1918-19 and was considered to have arrested pulmonary tuberculosis from 1925 to 1949 although acid fast bacilli were never recovered. In 1949, during the severest exacerbation he had experienced, Histoplasma capsulatum was repeatedly recovered in sputum cultures. Histoplasmin skin test was positive and coccidioidin and blastomycin were negative. The complement fixation test for histoplasmosis was positive. Right upper lobectomy was performed, although the pulmonary involvement was not entirely in this lobe.

Improvement with negative sputum and gain in weight followed prolonged treatment with Acti-dione which was effective when administered either intravenously (Upjohn) or orally (Lilly). Further investigation of Acti-dione in cases of histoplasmosis is indicated.

Acknowledgment: Frank Clifton, A.B., isolated the organisms and aided in preparation of the microphotograph.

RESUMEN

Se presenta un caso que tenía tos crónica después de "influenza" en 1918-19 y que era considerado como de tuberculosis detenida de 1925 a 1949 aunque nunca se encontraron bacilos ácido-resistentes. En 1949 durante la más severa de sus exacerbaciones se encontró histoplasma capsulatum en repetidos cultivos de esputos. La reacción cutánea de la histoplasmina fué positiva y la de la coccidioidina fué negativa. La reacción de fijación del complemento para la histoplasmosis fué positiva. Se llevó a cabo lobectomía superior derecha aunque la afección no estaba toda en ese lóbulo.

En seguida hubo mejoría con negativación del esputo y aumento de peso tras el uso de Acti-diona que fué efectiva administrada ya por vía intravenosa (Upjohn) u oral (Lilly). Está indicada la observación ulterior de casos de histoplasmosis tratados con Acti-diona.

*This patient was briefly referred to in the discussion of a recently published paper.[11]

RESUME

Les auteurs rapportent l'observation d'un cas de toux chronique à la suite "d'influenza" en 1918-19 qui fut considéré comme une tuberculose pulmonaire de 1925 à 1949, quoique des bacilles acido-résistants n'aient jamais été trouvés. En 1949, pendant l'évolution la plus grave que le malade ait éprouvée, on découvrit plusieurs fois par les cultures de crachats "l'histoplasma capsulatum." Le test à l'histoplasmine fut positif, et ceux à la coccidioidine et à la blastomycine furent négatifs. La réaction de fixation du complément pour l'histoplasmose fut positive. Une lobectomie supérieure droite fut pratiquée, malgré que l'atteinte pulmonaire ne s'étendit pas entièrement à ce lobe.

Un traitement prolongé à l'actidione fut suivi d'amélioration avec négativation des crachats, et gain du poids. Ce produit se montre efficace, aussi bien par voie intraveineuse (Upjohn) que par voie buccale. Les auteurs rapportent d'autres investigations sur l'action de l'actidione dans des cas d'histoplasmose.

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Report of the Council on Undergraduate Medical Education*

One of the most important and at the same time most overlooked factors in diseases of the chest has been the inadequacy with which this subject has been taught in medical schools. Consequently one of the primary objectives of the American College of Chest Physicians has been to assist medical schools in teaching this subject.

At the outset this Council made a study of the teaching of chest diseases in the medical schools of the United States and Canada. This study was carried out through questionnaires sent to the schools and by direct personal contact by members of the College. Guided primarily by the results of this survey and in response to requests from some schools for assistance, a schedule or outline for teaching diseases of the chest was formulated, the purpose of which was to serve as a guide in presenting this subject to the students.

This Council has been aware that those in charge of the curriculums of medical schools receive many demands for more time and consideration in the teaching of the various subjects. It was also realized that progress would be slow and that accomplishment would only be obtained by repeatedly calling the attention of medical deans or those responsible for arranging teaching programs to the importance of this particular subject and of the necessity for its more efficient teaching. In other words, on the premise that the philosophy of successful propaganda is repetition, an effort has been made by this Council, from the beginning of this work, to maintain contact with medical schools. In addition, the College of Chest Physicians through this Council has recently sponsored and published a book intended primarily for medical students and teachers. The purpose of this book is to present the fundamentals of pulmonary tuberculosis and its complications in as few concise chapters and as few well chosen words as possible. At present the College has another similarly arranged book on non-tuberculous conditions of the chest in preparation which will be published in the near future. Also this Council through invitation has during the past year prepared a manuscript on "Teaching Diseases of the Chest in Medical Schools" which was published in the May 1951, issue of the Journal of the Association of American Medical Schools.

*Presented at the 17th Annual Meeting, American College of Chest Physicians, Atlantic City, New Jersey, June 7, 1951.

It is logical to believe that the ideal of medical schools is to teach each subject or branch of medicine in direct proportion to its importance in the general field of medicine. From the studies made it has been felt that with very few exceptions the time allocated to teaching diseases of the chest has been sufficient and that the inadequacy of teaching in any particular institution is due to lack of teaching material or to an ineffective system of presenting this material.

It has been, and still is, the predominating consensus of those interested in diseases of the chest that pulmonary tuberculosis occupies the primary position of importance as a medical, public health and economic problem in this branch of medical practice. An efficient program for teaching diseases of the chest consequently must be developed so as to allow foremost consideration to pulmonary tuberculosis. It is at the same time realized that the teaching of non-tuberculous diseases of the chest must be given due consideration.

As has been emphasized at various times by this Council it is essential that each physician while in medical school be trained so that in practice he will be chest conscious and have an understanding that enables him to direct the patient with a chest condition intelligently. Unless this particular training is acquired in school it is only the rare physician that has any opportunity to be trained after graduation.

There still exists rather marked controversy in regard to the means by which the subject of diseases of the chest and particularly pulmonary tuberculosis can be efficiently taught. Deans of medical schools and professors of medicine, with relatively few exceptions, are rather persistent that this entire subject can and should be taught as an integral part of the course in internal medicine. On the other hand, those engaged in this particular field of medicine who are constantly reminded of the tragic failures to effectively teach this subject as a part of the course in internal medicine in the past are, with few exceptions, very definite in their conviction that diseases of the chest can be taught efficiently only when taught as an independent course.

One of the major difficulties in teaching diseases of the chest as a direct component of internal medicine is that under these circumstances there is a lack of interest and a lack of teaching facilities.

According to a recent report received by this Council from a large municipality regarded as an outstanding teaching center in which there are three medical schools, and two large tuberculosis sanatoria, the teaching of tuberculosis is frowned upon. There is apparently no harmony between the medical schools and the

sanatoria with the result that the sanatoria are not used in teaching and the student's instruction in clinical tuberculosis in two of these schools consists of three lectures only, one by a clinician, one by a chest surgeon and one by a radiologist. In the other school the report states that active teaching of tuberculosis has been given up. Non-tuberculous diseases of the chest in all of these schools is taught by a professor of internal medicine as a part of the internal medicine course.

From another part of the country the following report was received: "A check on the teaching of diseases of the chest at the two medical schools in this city will reveal a definite shortage of clinical material since discontinuance of an active tuberculosis ward at the County Hospital in this city, in 1946. The chest clinic out-patient department at each school affords little active material for physical examination; there is no treatment here. Diseases of the chest are taught as a part of general medicine by voluntary lectures. Time is available for only a few lectures. Assignments are in textbooks of general medicine and physical diagnosis. Both teaching hospitals prefer not to admit tuberculous patients."

Until recent years diseases of the chest were generally understood to comprise mainly, pulmonary tuberculosis and the pneumonias and their complications. Primarily due to increased diagnostic and therapeutic efficiency, diseases of the chest at the present time covers a wide field including more than 75 diseases or pathological states.

After much study and thought, due to the present magnitude of this subject and the great difference that exists in the factors pertaining to the teaching of diseases of the chest in medical schools, this Council concluded it should not at this time attempt to outline a detailed method for teaching this subject by revising the old schedule or formulating a new one. It is believed that it is more practical that, in addition to stressing the importance of diseases of the chest, to present a general outline of the basic factors in the diagnosis and treatment of diseases of the chest and the steps by which these factors can be most satisfactorily presented to medical students.

The University of Oregon Medical School has always been interested in the efforts of this Council. The report from this institution stated that, due to recent changes in their teaching system now in progress, didactic work for the most part will be given only in the junior year while the senior year will be occupied with institutional and bedside instruction.

Accompanying the report from this school was an outline of 27 lectures on diseases of the chest to be given during the junior year, sessions on the various phases of diseases of the chest to be con-

ducted one day a week. All this material is to be presented by teachers whose major experience has been in this particular field. Plans are also being made to include additional lectures on traumatic, esophageal, cardiovascular and other conditions of the chest.

In the present plan at the University of Oregon the seniors will have at least a two hour session each week for a minimum of six weeks. While this plan for teaching diseases of the chest at this school appears very encouraging, ideally it would be more satisfactory if the time spent by the senior medical students were spaced so that the students would have an opportunity not only to study but to observe the patients with chest conditions, particularly those with tuberculosis, throughout at least one school year.

In closing this report we would like to make a plea to the various chapters of the College and to the membership individually to support the work of this Council in its attempt to carry out this objective of the College. It would be possible for them to render this assistance by arousing due interest in the importance of diseases of the chest in present day medical practice and by rearousing those whose chief interests are in diseases of the chest to the recognition of the major problems in this field.

Appended will be found the present outline for the course of study of diseases of the chest at the University of Oregon Medical School. Also attached is the outline that was used in teaching diseases of the chest previous to the changes now being made at that school. This earlier outline is included with the thought that it may be of value to other schools that would not be able at this time to take the fullest advantage of more recent plans.

Edward W. Hayes, M.D., Chairman
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Foster Murray, M.D.
Brooklyn, New York
Eli H. Rubin, M.D.
New York, New York
Moses J. Stone, M.D.
Boston, Massachusetts

OUTLINE OF LECTURES IN DISEASES OF THE CHEST

1. Introduction: Normal lung defenses, important physiological considerations in diseases of the chest.
2. Introduction: Normal lung defenses, important physiological considerations in diseases of the chest.

3. Acute common respiratory disease.
4. Pneumonia—bacterial and viral.
5. Pneumonia—bacterial and viral.
6. Bronchial obstruction: Effects, recognition, causes (foreign body, adenoma, stricture, carcinoma and other tumors).
7. Bronchial obstruction: Effects, recognition, causes (foreign body, adenoma, stricture, carcinoma and other tumors).
8. Bronchopulmonary suppuration — bronchitis, bronchiectasis, lung abscess.
9. Bronchopulmonary suppuration — bronchitis, bronchiectasis, lung abscess.
10. Intrathoracic tumors.
11. Intrathoracic tumors (details of surgical treatment not to be considered).
12. Epidemiology and pathogenesis of tuberculosis.
13. Epidemiology and pathogenesis of tuberculosis.
14. Clinical types, reaction and cause of tuberculosis (infiltrates, pneumonias, cavity formation, fibrosis, etc.).
15. Clinical types, reaction and cause of tuberculosis (infiltrates, pneumonias, cavity formation, fibrosis, etc.).
16. Medical principles of the treatment of tuberculosis.
17. Medical and surgical principles of treatment of tuberculosis. Prognosis.
18. Special tuberculous lesions; laryngitis, bronchitis, etc.
19. Diagnosis and management of tuberculous pleural effusion.
20. Empyema.
21. Bronchial asthma (and effect), emphysema, lung cysts, spontaneous pneumothorax, mediastinal emphysema.
22. Bronchial asthma (and effect), emphysema, lung cysts, spontaneous pneumothorax, mediastinal emphysema.
23. Sarcoidosis.
24. Fungus diseases of the lung.
25. Pneumonoconiosis.
26. Interpretation of cough, chest pain and hemoptysis.
27. Interpretation of cough, chest pain and hemoptysis.

Medicine 628

DISEASES OF THE CHEST:

LECTURES AND DEMONSTRATIONS

Tuberculosis Hospital Tuesday at 8 a.m. throughout the year.

1. History Taking and Symptomatology in Diseases of the Chest.
2. Physical Diagnosis in Diseases of the Chest.
3. X-ray Diagnosis in Diseases of the Chest.
4. Special Diagnostic Procedures.
5. Differential Diagnosis in Diseases of the Chest.
6. Epidemiology of Pulmonary Tuberculosis.
7. Pathogenesis of Pulmonary Tuberculosis.
8. Diagnosis and Classification of Pulmonary Tuberculosis.
9. and 10. General Medical Treatment of Tuberculosis.

Q U I Z :

11. Pathological Physiology in Diseases of the Chest.
12. Pneumothorax and Its Complications.
13. Intrapleural Pneumonolysis.
14. Phrenic Nerve Interruption and Pneumoperitoneum.
15. Thoracoplasty and Apicolysis.
16. Extrapleural Procedures and Pulmonary Resection for Tuberculosis.
17. Complications of Tuberculosis and Factors Affecting Prognosis in Pulmonary Tuberculosis.
18. Pleural Effusions.
19. Empyema.
20. Streptomycin Therapy.

Q U I Z :

21. The Pneumonoconioses and Lipoid Pneumonia.
22. Fungus Diseases of the Lungs.
23. and 24. Pulmonary Suppurations.
25. and Intrathoracic Tumors.
27. Diseases of the Esophagus.
28. Surgery of the Heart and Great Vessels.
29. Surgery of the Diaphragm and Chest Wall.
30. Chest Trauma.

PRELIMINARY PROGRAM

Eighteenth Annual Meeting

American College of Chest Physicians

Congress Hotel, Chicago, Illinois

JUNE 5 - 8, 1952

THURSDAY, JUNE 5

9:00 a. m. Oral Examinations
10:00 a. m. Annual Meeting, Board of Governors
12:00 noon Luncheon, Conference of College Chapter Officials
2:00 p. m. Annual Meeting, Board of Regents
2:00 p. m. Written Examinations

Councils and Committees of the College will hold their Annual Meetings on Thursday, June 5.

There will be special meetings of the Council on Undergraduate Medical Education and the Council of Tuberculosis Hospitals.

8:00 p. m. Scientific Session:

"The Diagnosis of Cardiospasm,"
Arthur M. Olsen and Colin B. Holman, Rochester, Minnesota.

"Artificial Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis,"
Francisco J. Menendez, Havana, Cuba.

"Tuberculous Pneumonia in the Negro,"
Sydney Jacobs, New Orleans, Louisiana.

"Hotchkiss-McManus Stain for Demonstrating Fungi in Tissue,"
J. Winthrop Peabody, Jr., New Orleans, Louisiana.

"Relationship of Incidence of Emboli in Acute Coronary Artery Occlusion to Treatment,"
R. W. Kissane, Columbus, Ohio.

FRIDAY, JUNE 6

9:00 a. m. - 12:00 noon:

"Pulmonary Ventilatory Function Tests and Clinical Application,"
Maurice S. Segal, Boston, Massachusetts, Chairman.

"Some Problems of Bronchospirometry—Analysis of 724 Procedures,"
Edward A. Gaensler, Boston, Massachusetts.
Discussion: George W. Wright, Saranac Lake, New York.

"The Use of Pulmonary Function Tests in Evaluating Disability in Coal Miners,"
Hurley L. Motley, Philadelphia, Pennsylvania.
Discussion: George W. Wright, Saranac Lake, New York.

"Pulmonary Function and Circulatory Dynamics in Artificial Pneumoperitoneum,"
Ross C. Kory, Dan C. Roehm and George R. Meneely, Nashville, Tennessee.
Discussion: Hurley L. Motley, Philadelphia, Pennsylvania.

"Differentiation of Pulmonary Fibrosis and Pulmonary Emphysema by Physiologic Standards,"
George W. Wright, Saranac Lake, New York.
Discussion: Edward A. Gaensler, Boston, Massachusetts and George R. Meneely, Nashville, Tennessee.

Intermission — 10 minutes.

Panel Discussion: Maurice S. Segal, Chairman
Edward A. Gaensler
George R. Meneely
Hurley L. Motley
George W. Wright.

12:00 noon Round Tables

There will be six Round Table Luncheon Meetings on topics of current interest.

2:00 p. m. - 5:00 p. m.

Cardiovascular Diseases
Charles P. Bailey, Philadelphia, Pennsylvania, Chairman
Nathaniel E. Reich, Brooklyn, New York, Co-chairman.

"Revascularization of the Heart,"
Claude S. Beck, Cleveland, Ohio.

"Newer Methods of Cardiovascular Diagnosis,"
Myron Prinzmetal *et al.*, Los Angeles, California.

"The Differentiation of Cardiac and Pulmonary Lesions by Angiocardiography,"
Charles T. Dotter, New York, New York.

Panel Discussion: Charles P. Bailey, Chairman
Nathaniel E. Reich, Co-chairman
Claude S. Beck
Charles T. Dotter
Myron Prinzmetal.

8:00 p. m. - 10:00 p. m.

Motion Picture Session on Diseases of the Chest
Paul H. Holinger, Chicago, Illinois, Chairman.

SATURDAY, JUNE 7

10:00 a. m. - 12:00 noon

Occupational Diseases of the Chest

A series of short presentations on topics of current interest in the field, followed by a Panel Discussion with questions from the floor.

O. A. Sander, Milwaukee, Wisconsin, Chairman
Louis L. Friedman, Birmingham, Alabama, Co-chairman
Arthur J. Vorwald, Saranac Lake, New York, Co-chairman.

12:00 noon Round Tables

There will be six Round Table Luncheon Meetings on topics of current interest.

2:00 p. m. - 3:00 p. m.

"Causes of Death in Carcinoma of the Lung in a Large Public Hospital,"
Frederick F. Boyce, New Orleans, Louisiana.

"Environment and Cancer of the Lung,"
Stelio Imprescia, Louisville, Kentucky.

"Nonsurgical Treatment of Cancer of the Lung,"
Edgar Mayer, New York, New York.

3:00 p. m. - 3:30 p. m.

"The Reliability of Chest Roentgenography and Its Relation to Clinical Disease,"
Jacob Yerushalmy, Berkeley, California.

3:30 p. m. - 5:00 p. m. X-ray Symposium

Leo G. Rigler, Minneapolis, Minnesota, Chairman.

6:00 p. m. Convocation

7:00 p. m. Cocktail Party and the Annual Presidents' Banquet
Award of the College Medal

SUNDAY, JUNE 8

9:00 a. m. - 12:00 noon

Medical Management of Diseases of the Chest,

W. L. Howard, Northville, Michigan, Chairman.

"The Place of Pneumoperitoneum in the Nonsurgical Treatment of Pulmonary Tuberculosis,"
William Schwartz, Oteen, North Carolina.

"Long Term Streptomycin Therapy Program Without Collapse,"
Nicholas D. D'Esopo, Sunmount, New York.

"Bed Rest,"
William M. Peck, McCain, North Carolina.

"The Place of Pneumothorax Treatment in Pulmonary Tuberculosis,"
Roger S. Mitchell, Trudeau, New York.

"The Place of Phrenic Paralysis in the Treatment of Pulmonary Tuberculosis,"
W. F. Fidler, Howell, Michigan.

"Antimicrobial Therapy of Pulmonary Tuberculosis,"
William B. Tucker, Minneapolis, Minnesota.

Panel Discussion: W. L. Howard, Chairman
Nicholas D. D'Esopo
W. F. Fidler
Roger S. Mitchell
William M. Peck
William Schwartz
William B. Tucker
B. H. Wardrip.

12:00 noon Round Tables

There will be six Round Table Luncheon Meetings on topics of current interest.

2:00 p. m. - 5:00 p. m.

Surgical Management of Diseases of the Chest,
Herbert C. Maier, New York, New York, Chairman.

"Segmental Resection in Tuberculosis,"
Richard H. Overholt, Francis M. Woods and Norman J. Wilson, Brookline, Massachusetts.

"Pulmonary Resection for Tuberculosis in Children and Adolescents,"
Morris Rubin, Bronx, New York.

"Cystic Disease of the Lung,"
Richard H. Meade, Jr. and Richard Rasmussen, Grand Rapids, Michigan.

Panel Discussion: Herbert C. Maier, Chairman
Richard H. Meade, Jr.
Richard H. Overholt
Morris Rubin.

6:00 p. m. Open House

College Building,
112 East Chestnut Street, Chicago, Illinois.

Members are requested to obtain their hotel reservations for the annual meeting at once. Reservations may be made by writing directly to the Congress Hotel, Chicago 5, Illinois.

Amendments to the By-Laws

American College of Chest Physicians

The following amendments to the College By-Laws were approved by the Board of Regents at their semi-annual meeting held in Los Angeles, California, December 3, 1951. These amendments will be voted upon by the membership of the College at the administrative session of the annual meeting in Chicago on June 7, 1952.

ARTICLE III, Section 3 (b)

Present wording:

(b) He shall be a member in good standing of his local, state, and national medical societies, provided, however, that if he is

(1) a full time teacher or research worker in a hospital or institution acceptable to the Board of Regents;

(2) a medical officer in the service of the United States Government, or

(3) engaged solely in the public welfare service,

the requirement of membership in a local, state or national medical society may be waived by the Governor, Regent and Chairman of the Board of Regents upon a consideration of his application, as provided in Section 7 of this Article III.

Changes Recommended:

He shall be a member in good standing of his county medical society or the American Medical Association, provided, however, that if he is

(1) a full time teacher or research worker in a hospital or institution acceptable to the Board of Regents;

(2) a medical officer in the service of the United States Government, or

(3) engaged solely in public welfare service,

the requirement of membership in a county medical society or the American Medical Association may be waived by the Governor, Regent and Chairman of the Board of Regents upon a consideration of his application, as provided in Section 7 of this Article III.

ARTICLE X, Section 4 (a)

Present wording:

(a) The following councils, consisting of nine members each, shall be appointed:

Council on Undergraduate Medical Education,
Council on Postgraduate Medical Education,
Council on Public Health,
Council of Tuberculosis Hospitals,
Council of Tuberculosis Committees,
Council on the Management and Treatment of Diseases of the Chest,
Council on Public Relations.

At the first appointment of these councils three of such members shall be appointed for a one-year term, three for a two-year term, and three for a three-year term. Every year thereafter three members shall be appointed for a three-year term.

Changes Recommended:

(a) The following councils, consisting of nine members each, shall be appointed:

Council on Undergraduate Medical Education,
Council on Postgraduate Medical Education,
Council on Hospitals,
Council on Research.

At the first appointment of these councils three of such members shall be appointed for a one-year term, three for a two-year term, and three for a three-year term. Every year thereafter three members shall be appointed for a three-year term.

ARTICLE X, Section 4 (c)

It is recommended that this section, covering the composition of the Council on Research, be eliminated from the by-laws and that Section 4 (d) be changed to Section 4 (c).

ARTICLE X, Section 6

It is recommended that the Committee on Public Relations be added to this list of standing committees.

Plans Progressing for Two World Congresses in Rio de Janeiro

Arrangements are progressing rapidly for the XII Congress of the International Union Against Tuberculosis and the II International Congress on Diseases of the Chest sponsored by the Council on International Affairs of the American College of Chest Physicians which are to be held in Rio de Janeiro, Brazil, August 24 through 30, 1952. The scientific programs to be presented at the two World Congresses are being organized and it is anticipated that a preliminary program will appear in an early issue of the journal.

Professor Etienne Bernard, Secretary General, International Union Against Tuberculosis, 47 Rue de Courcelles, Paris, France, is in charge of the program on tuberculosis subjects and Dr. Andrew L. Banyai, Chairman, Council on International Affairs, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, is organizing the program on nontuberculous subjects, to include heart and lung disease. Physicians who wish to present papers in the scientific program of the Rio Congresses are invited to write directly to the appropriate program chairman.

Reservations are now being received from members who wish to participate in the College "flying congress" which is to take place in the air during the flight to Rio de Janeiro. This will be a "first" in the history of medicine; a scientific program on diseases of the chest presented in the sky. Arrangements have been completed with Pan American World Airways for this flight on their world famous Stratocruiser, "El Presidente" leaving New York City at 11:00 a. m. Thursday, August 21. Actual flying time to Rio de Janeiro is 19 hours. Members who wish to participate in the "flying congress" are urged to make reservations at once, as the space on this flight will be assigned in the order in which requests are received. Please write to the Executive Offices of the College in Chicago for reservations and further information.

New Jersey Postgraduate Course

The first annual postgraduate course in diseases of the chest for the general practitioner has been arranged under the auspices of the New Jersey Chapter of the College and the New Jersey Academy of General Practice. This postgraduate course is being sponsored by the Council on Postgraduate Medical Education of the American College of Chest Physicians.

The sessions will be held on four consecutive Wednesdays commencing February 20 and will continue through March 12, 1952. All sessions will be given at the Essex House Hotel, 1050 Broad Street, Newark, New Jersey. The following physicians comprise the postgraduate course committee:

J. R. Herradora, Director

Irving Willner, Chairman	Samuel Cohen, Secretary
Felix Baum	A. Joseph Hughes
Frank Bortone	Lester L. Klapper
Albert Carabelli	Marcus Newcomb
Martin Castellano	Albert A. Peckman
Homer Cherry	Allan J. Stolow

Lawrence A. Wilson

The co-ordinators for this course are: Edwin Rosner, President-Elect; Vincent Campana, Vice-President; Arthur Trewhella, Secretary-Treasurer, of the New Jersey Academy of General Practice; Juan R. Herradora, President, New Jersey Chapter of the American College of Chest Physicians; and Irving Willner, Governor of the College for New Jersey.

Sixteen hours of formal credit toward postgraduate education requirements of the New Jersey Academy of General Practice will be given to the physicians completing this course.

Philadelphia Postgraduate Course

The Fifth Annual Postgraduate Course in diseases of the chest sponsored by the Council on Postgraduate Medical Education of the College and the Laennec Society of Philadelphia will be held at the Warwick Hotel, Philadelphia, Pennsylvania, March 24-28, 1952. The members of the Executive Committee in charge of the postgraduate course are:

Chevalier L. Jackson, Chairman

Katharine R. Boucot	Burgess L. Gordon
Leon H. Collins, Jr.	Esmond R. Long
J. Antrim Crellin	Charles M. Norris

Martin J. Sokoloff

J. Winthrop Peabody, ex-officio

An interesting program on the newer aspects of diseases of the chest has been prepared for this postgraduate course. The program includes sessions on cardiovascular disease, cardiovascular surgery, impact of streptomycin on the problem of tuberculosis, ACTH and Cortisone in tuberculosis, roentgenology and the chest, "B.C.G." diagnosis of esophageal disease, surgery of the esophagus, fungus of the lung, suppurative diseases of the bronchi and lung, and bronchopulmonary tumors.

College Chapter News

CUBAN CHAPTER

Dr. Chevalier L. Jackson, President of the American College of Chest Physicians was honored by the Cuban Chapter of the College during his visit to Cuba, January 20-24. Dr. Jackson was the guest of honor of the III Pan American Congress of the International Society for Otorhinolaryngology.

At the opening of the Congress, Dr. Jackson received a certificate from the Pan American Colombist Society for his many years of devoted service to the Latin American countries in the field of medicine.

The congress was presided over by Dr. Jose Gros. Members of the Cuban Chapter of the College participating were Dr. Pedro Hernandes, Secretary, Dr. Rufino Moreno, and Dr. Jose Garcia Arrazuria.

Dr. Jackson presented a lecture on "Peroral Endoscopy" which was discussed by Dr. Hernandes and Dr. Antonio Navarrete.

College members from other countries who attended the congress as delegates: Drs. Carlos Rodrigues Moraes, Brazil; Valmore Latraverse, Canada; Enrique Ortega M., Ecuador; Ricardo Tapia Acuna, Mexico; and Paul H. Holinger, United States of America.

At the end of the congress a special session was held under the auspices of the Cuban Chapter in which the paper entitled "Postoperatory and Posttraumatic Pulmonary Atelectasis" was presented by Dr. Carlos Stajano of Montevideo, Uruguay. This meeting was presided over by Dr. Antonio Rodriguez Diaz. The following are the new officers of the chapter:

Antonio Rodriguez Diaz, President
Ricardo Sanchez Acosta, Vice-President
Francisco Perez Carballas, Secretary-Treasurer.

Antonio Navarrete, Regent.

NEW JERSEY CHAPTER

The annual spring meeting of the New Jersey Chapter of the American College of Chest Physicians will be held on Tuesday, May 20, 1952 at the Chalfonte Hotel, Atlantic City, New Jersey. This meeting will take place during the Annual Meeting of the New Jersey State Medical Society.

Dr. Martin Sokoloff, Associate Professor of Medicine, Jefferson Medical College, Philadelphia, and Acting Medical Director, Barton Memorial Division of Jefferson Hospital, will speak at the luncheon meeting. He will talk on "Recent Advances in Our Knowledge of Pulmonary Emphysema."

Irving J. Selikoff, Secretary.

NEW YORK CHAPTER

The 12th annual meeting of the New York State Chapter of the College was held at the Hotel New Yorker, New York City, on February 21.

The annual dinner meeting of the chapter to be held in conjunction with the Annual Meeting of the Medical Society, State of New York, will take place at the Statler Hotel, New York City, on Thursday evening, May 15.

ILLINOIS CHAPTER

The Illinois Chapter of the College held a joint meeting with the Chicago Roentgen Society at the University Club, Chicago, Illinois, on Thursday, February 14. A symposium on "Superior Vena Caval Syndrome" was presented, and the following panel members participated in the discussion: Drs. Leo Latz, Israel Kirsh, G. O. Ornbreck, Harry Cooper, Paul Alfano, and Eric Uhlmann.

Closing remarks were made by Dr. Warren Furey, past president of the Chicago Medical Society.

On March 14, the Illinois Chapter will present a program which is being prepared by the chest and thoracic surgery departments of the University of Chicago. On April 4, there will be a joint meeting of the Illinois Chapter of the College and the Chicago Diabetes Association.

Abel Froman, Secretary-Treasurer.

MISSOURI CHAPTER

A joint meeting of the Missouri Chapter of the American College of Chest Physicians and the Missouri Trudeau Society will be held at the Jefferson Hotel, St. Louis, Missouri, March 30, 1952, at 12 noon. Following the luncheon, a scientific program will be presented:

Round Table Discussion: "Valvulotomy," D. B. Flavan, Chairman, C. Rollins Hanlon, Thomas Burford, and B. C. Bercu, St. Louis, Mo.

"Cineradiograph in the Study of Thoracic Lesions,"
Osler Abbott, Emory University Medical School, Atlanta, Georgia.

"Anthracosilicosis,"
Louis L. Friedman, Birmingham, Alabama.

Discussion: Emmett F. Pearson, Springfield, Illinois.

"Azotemic Edema of the Lung and Its Relationship to Collagen Disease,"
L. R. Sante, St. Louis, Missouri.

Discussion: Stanley Hampton, St. Louis, Missouri.

Alexander J. Steiner, Secretary.

NEW ENGLAND CHAPTER

The following is a list of the conferences held during the past few months and those planned for the spring of 1952, sponsored by the New England Chapter, American College of Chest Physicians, and the Overholt Clinic. These sessions are held at the Deaconess Hospital, Boston, Massachusetts:

October 17, 1951: Edward Gaensler, "Pulmonary Functional Studies."

November 21, 1951: Case Presentations.

December 19, 1951: Maurice Segal, "Recent Advances in the Treatment of Pulmonary Emphysema."

January 17, 1952: Laurence L. Robbins, "The Roentgen Anatomy and Identification of Mediastinal and Pulmonary Lymph Nodes."

February 21, 1952: Theodore Badger, "Relapse in Pulmonary Tuberculosis."

March 19, 1952: Robert Fienberg, "Non-specific Granulomas."

April 16, 1952: Norman J. Wilson, "Results of Pulmonary Resection in Tuberculosis."

May 21, 1952: Philip Schwartz, "The Role of Intrathoracic Lymph Nodes in the Pathogenesis of Pulmonary Tuberculosis."

WISCONSIN CHAPTER

The Metropolitan Section of the Wisconsin Chapter of the College met at the Medford Hotel, Milwaukee, on Friday, January 25. "The Evaluation of Patients for Surgery of Acquired Heart Disease" was presented by Dr. Timothy R. Murphy.

College News Notes

The College News Section of *Diseases of the Chest* is devoted to the activities of the members. Kindly send all news items to the American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.

Dr. Daniel C. Braun, Pittsburgh, Pennsylvania, has been appointed medical director of the Industrial Hygiene Foundation and simultaneously takes up his duties as lecturer in occupational health at the University of Pittsburgh Graduate School of Public Health.

The announcement of Dr. Braun's new appointment was made jointly by Dr. Thomas Parran, dean of the graduate school, and Dr. C. Richard Walmer, managing director of Industrial Hygiene Foundation.

Dr. Braun has been medical director of the Pittsburgh Coal Company since 1944. He also served as advisor to Westinghouse Electric Corporation in its supervisory health program.

Dr. Braun succeeds Dr. C. Richard Walmer in this position. Dr. Walmer has been promoted to the position of managing director of the Industrial Hygiene Foundation.

Dr. Basil A. Dormer, Durban, South Africa, Secretary of the Council on African and Eastern Affairs of the American College of Chest Physicians, and Dr. W. Cotter Harvey, Sydney, Australia, Regent of the College for Australia, have been appointed as members of the editorial board of the *British Journal of Tuberculosis and Diseases of the Chest*.

Dr. Samuel Topperman, formerly Assistant Medical Director of the New York City Municipal Tuberculosis Sanatorium, Otisville, New York, has been appointed Medical Superintendent of the East Texas Tuberculosis Sanatorium, Tyler, Texas.

Dr. Robert Locke, Reno, Nevada, has accepted appointment by the President of the College, Dr. Chevalier L. Jackson, as Governor of the American College of Chest Physicians for the State of Nevada.

COLLEGE EVENTS

18th Annual Meeting, American College of Chest Physicians, Congress Hotel, Chicago, Illinois, June 5-8, 1952.

Illinois Chapter Meeting, Chicago, March 14 and April 4, 1952.

New Jersey Postgraduate Course, Newark, February 20 - March 4 (four consecutive Wednesdays).

Philadelphia Postgraduate Course, March 24-28, 1952.

Missouri Chapter Meeting, St. Louis, March 30, 1952.

Texas Chapter Meeting, Dallas, May 5, 1952.

New Jersey Chapter Meeting, Atlantic City, May 20, 1952.

XII Congress, International Union Against Tuberculosis
II International Congress on Diseases of the Chest
Rio de Janeiro, Brazil, August 24-30, 1952.

Chicago Postgraduate Course, October 6-10, 1952.

New York Postgraduate Course, November 10-15, 1952.

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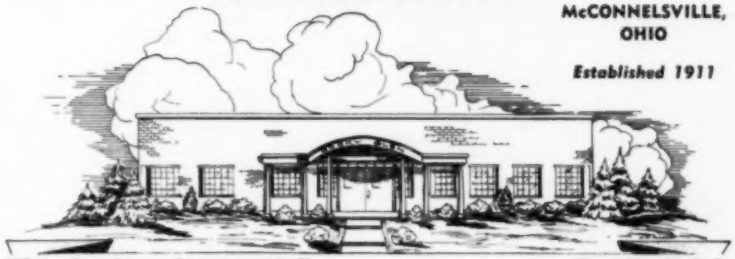

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POSITIONS AVAILABLE

Medical director wanted for tuberculosis hospital at a salary of $4,820.00 per year and full maintenance. Please address Box 241A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Two residents wanted for 175 bed Ohio tuberculosis hospital approved for residency. Salary $250.00 per month less nominal charge for maintenance. Single physician preferred. One vacancy April 1, 1952. One vacancy June 10, 1952. Please address Box 242A, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.

Assistant Medical Director in 225 bed tuberculosis sanatorium. For details please write Jefferson Tuberculosis Sanatorium, 3800 Montgomery Highway, Birmingham 9, Alabama.

Assistant medical director for 600 bed hospital in South Central state. Salary $7,500 per year, plus complete maintenance. Graduate of American Medical School desired; well rounded training in tuberculosis required. Please address Box 243A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Staff physician wanted for Ohio county tuberculosis hospital. Experience in tuberculosis and Ohio State License necessary. Salary $7,000 to $8,000, plus furnished house. Apply to Box 244A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

POSITIONS WANTED

Thoracic and general surgeon, age 34, has seven years' training, two in thoracic surgery including tuberculosis. Passed Part I Surgery. Available in July. Desires association, partnership, institutional appointment with opportunity for private practice. Please address Box 261B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Thoracic surgeon, age 36, certified American Board of Surgery, eligible Board of Thoracic Surgery, desires full or part time position in sanatorium or group. Vast experience in modern tuberculosis and general thoracic surgery. Outstanding references. Please address Box 262B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Chest specialist, age 35, F.C.C.P., eligible board on internal medicine, desires responsible position in or near large city with group, associate, or sanatorium. Available July 1952. Excellent references. Please address Box 263B, American College of Chest Physicians, 112 East Chestnut St., Chicago 11, Illinois.

NEWS RELEASE

The availability of Pasara Calcium Granulate, the calcium salt of para-aminosalicylic acid, has been announced by George Underwood, M.D., medical director of the Smith-Dorsey Division of The Wander Company.

Pasara Calcium makes available for the first time the calcium salt of PAS. Supplied in the form of granules coated with a sialoresistant substance, Pasara Calcium provides 85 per cent calcium para-aminosalicylate or 75 per cent of the free acid.

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Histoplasmosis must be taken into account in all routine x-ray surveys of population and differentiated from tuberculosis despite superficial similarities. Carefully controlled studies of the etiology of histoplasmosis in relation to conditions that vary geographically are very much needed. G. Arnold Cronk, M.D., N.Y.S. J. of Medicine, August 15, 1951.

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REFERENCES: 1. "Current Status of Antimicrobial Therapy," Am. Rev. Tuberculosis, 1951, 63, 573. 2. Cutler, J. W., Extrapleural Pneumothorax in Collapse Therapy," J. Thoracic Surg., 1951, 21, 217. 3. "Meningeal and Acute Miliary Tuberculosis," Trans. 10th VA Conference Chemotherapy of Tuberculosis, January 1951, pp. 368-369.

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